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JAMES C. MUNCH.

James Clyde Munch, Second Vice-President of the AMERICAN PHARMACEUTICAL ASSOCIATION, was born in Farmer City, Ill., in 1896. After receiving a B.S. in 1915, and an M.S. in Toxicology from Illinois Wesleyan Western University, Bloomington, Ill., in 1916, the following year was spent in dye research, and in teaching organic and physiological chemistry at the University of Louisville Medical School. Joining the Bureau of Chemistry U. S. D. A., as a physical chemist, studies on measurement of volume and shrinkage were interrupted by the World War. A commission in the Sanitary Corps, and a year overseas with the Seventh and Ninety-First Divisions, were followed by a return to the Bureau of Chemistry, with transfer to the Pharmacology Laboratory. Researches on red squill and thallium were undertaken for the Bureau of Biological Survey. Studies on the development of bioassays were started, in association with the recognition of bioassays in U. S. P. X. In 1924 George Washington University awarded him the degree of Doctor of Philosophy for studies on the Meyer-Overton theory of narcosis.

He has been a member of the faculty of Temple University since 1932, teaching physiology, pharmacology and bioassays, and directing research. After serving as director of Pharmacological Research for Sharp & Dohme, he is now director of Division of Tests and Standards, John Wyeth & Brother.

He has served as chairman of the Scientific Section of the AMERICAN PHARMACEUTICAL ASSOCIATION, 1928–1929; chairman of the Committee on Physiological Testing; and a member of the Committee on Pharmaceutical Research, as well as other committees. He is the chairman of the Committee on Pharmacology and Bioassays of the National Conference on Pharmaceutical Research. He served as an auxiliary member of the Revision Committees of U. S. P. X, U. S. P. XI and N. F. VI, and has been appointed a member of the Revision Committee of R. B. II. He is the chairman of the Section on Queries and Papers of the Pennsylvania Pharmaceutical Association. In addition to two books on bioassays, he has published about 125 papers on bioassays, toxicology and pharmacology.

EDITORIAL

E. G. EBERLE, EDITOR 2215 Constitution Ave., WASHINGTON, D. C.

EDUCATION FOR PROFESSIONS.

DR. JAMES ROWLAND ANGELL, of Yale, has fostered specialized research because "nobody knows what particular line of study may prove to have practical value." This has been shown in the results of education in pharmacy, represented by outstanding figures in various activities. These individuals have heretofore been referred to because of their association with pharmacy in early or late periods of life and who achieved greatness in one or the other or more of the divisions that contribute to pharmaceutical education. This is also in evidence by some who have been educated in pharmacy and, thereafter, observations in other fields, to which they have been directed, were enabled to apply their training advantageously in these activities. Here we have synthesis applied in the building up of an educational system and an analysis for applying a division of it. In pharmaceutical education and training an essential effort is effective coördination of its divisions, so that all may lead to a common end in preparing young men and women for service in the profession.

In speaking of the departments of a university Dr. Angell states "these should be synthesized and integrated and 'the intellectual parochialism' that tends to split up a university into disrelated and jealous parts," should be discouraged.

Can the foregoing be applied to pharmacy schools? Naturally, the aim is to devote more attention to one or the other division and students seek an institution, because of this, but the aim should be to prepare the students for pharmaceutical practice. The thought may extend beyond the school in selecting the future pharmacists, which is of great importance to the profession and the public. The attitude of the pharmacist to his profession is quite as important as his intelligent equipment for the practice of pharmacy.

PROFESSIONAL ETHICS.

THE STANDARD of a profession depends on the individuals who comprise the constituency; its promotion is hindered, however few their number may be, by those who thoughtlessly or selfishly are unmindful of its precepts. No profession is free from selfish and sordid minds and their influences concern all engaged and, particularly, those who are charged with the duties of selection and supervision. Environment may hinder, association may discourage them, temptations may surround them with allurements; it calls for power in judgment, determination to do right and nobility of thought. These officials are selected with the thought of public service and professional advancement and betterment—to this end all pharmacists, state and city officials and citizens, in so far as their ability enables them to judge, have a part, because of the importance of right practice in public health matters.

It could not be expected that pharmaceutical practice has been entirely free from dereliction, and charges of malpractice by those in authority is made with a knowledge of the facts that warrant the accusations, and when the facts are known there

should be no hesitancy nor delay in correcting the conditions to the end that the public may realize that pharmacists are jealous of the responsibilities placed upon them and the good name of pharmacy.

This comment has been prompted by certain developments made known by state press and other publicity. If the charges are not proven, amends as far as possible are in order; if true, as seems to be a lamentable fact in this case, the effort begun some time ago by the National Association of Boards of Pharmacy and THIS ASSOCIATION should be given unswerving earnest support and the officials commended for their courage in the discharge of their duties.

THE LEAGUE OF NATIONS AND CONTROL OF TRAFFIC IN OPIUM AND OTHER DANGEROUS DRUGS.

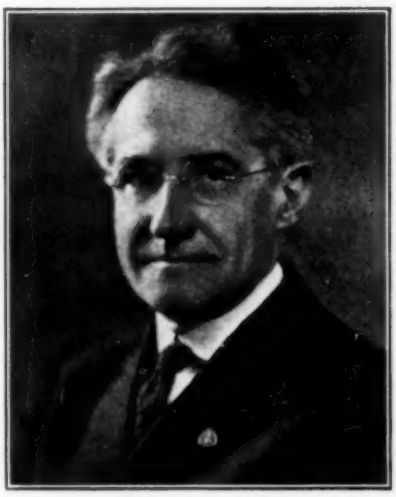
COMMISSIONER H. J. ANSLINGER has reported on the draft of rules recommended for the control of pharmacies by the Advisory Committee on Traffic in Opium and Other Dangerous Drugs, League of Nations at Geneva, June 1, 1937.

The Commissioner states that "these rules are practically all in effect in the United States with the exception of the limitations on the quantity of narcotic drugs to be purchased in any one year and the limitations on stocks of such drugs in the possession of pharmacies."

The AMERICAN PHARMACEUTICAL ASSOCIATION has given support and assistance in the preparation of regulations by Commissioner Anslinger and the report exhibits a conformity of thought in the preparation of the report and the regulations which obtain in this country.

The limits referred to by the Commissioner are embodied in the following:

"These limits should take into consideration the requirements of each pharmacy as based on its normal bona fide business, with provisions for additional allowances if justified by special circumstances."



CHARLES H. LaWALL.

The President and the Local Secretary of the New York A. PH. A. meeting, 1919.

Left, Charles H. LaWall, Philadelphia, *President*.

Right, Hugo H. Schaefer, *Local Secretary*, 1919 and 1937.

The sessions of the ASSOCIATION were held in Hotel Pennsylvania, beginning August 26, 1919.

HUGO H. SCHAEFER.

SCIENTIFIC SECTION

BOARD OF REVIEW OF PAPERS.—*Chairman*, F. E. Bibbins; H. M. Burlage, W. G. Crockett, E. V. Lynn, C. O. Lee, L. W. Rising, L. W. Rowe, Heber W. Youngken, F. V. Lofgren, J. C. Krantz, Jr.

PHENOL RESISTANCE OF STAPHYLOCOCCUS AUREUS.*

BY E. E. VICHER, ESTHER MEYER AND E. N. GATHERCOAL.[1]

The phenol resistance of fourteen oral and five stock strains of *Staphylococcus aureus* was determined using the F. D. A. method.

The results of this series of determinations show that the various strains of *Staphylococcus aureus* tested display marked differences in their resistance to phenol as well as a day to day variation in resistance of the individual strains.

In determination of phenol coefficient values, the most important factor influencing the final results is the resistance of the organism used in the test.

In dealing with agents such as antiseptic mouthwashes and others intended for personal use, the United States Food and Drug Administration recommends *Staphylococcus aureus* as the standard organism to be used, and in the monograph on Antiseptic Solution N. F. VI, the test for the determination of the antiseptic value of the solution employs this organism.

HISTORICAL.

The variability of *Staph. aureus* in its resistance to phenol was shown by Smyth (1934) and an evaluation of certain factors influencing this resistance may be found in his work with *Staph. aureus* A-209, the F. D. A. strain used in disinfectant testing.

Miller (1920) found this day to day resistance of the organism was the chief factor influencing his work.

Knaysi and Gordon (1930), using the same strain under identical conditions, experienced the same difficulty in disinfectant testing.

Systematic tests on the efficiency of germicidal agents were first conducted by Koch in 1881, followed by new methods or modifications by Esmarch in 1887, Henle in 1889, Fraenkel in 1889, Behring in 1890, Geppert in 1889, Gruber in 1891, Kronig and Paul in 1897, Rideal and Walker in 1903, Madsen and Nyman in 1907, Chick and Martin in 1908, the Lancet Commission in 1909, Anderson and McClintic in 1911, and many others.

The Anderson-McClintic method, commonly known as the Hygienic Laboratory or H-L method, as well as the Rideal-Walker method were used in various government laboratories in Washington up to the time that Shippen (1916) advanced his modified method which uses the best features of the two formerly accepted tests.

Reddish (1927) and Brewer and Reddish (1929) published this method, now known as the "R-W Modified Method," and it is included in detail in Circular No. 198, U. S. Dept. Agriculture (1931) by Ruehle and Brewer.

Meyer and Gathercoal (1936) present a slight modification of the F. D. A. standard. They found during extensive studies in the preparation of a test to determine the antiseptic value of Antiseptic Solution, N. F. VI, that very rarely did a strain of *Staph. aureus* meet the resistance requirements of the F. D. A. standard.

TECHNIQUE.

The method used in the determination of phenol resistance of the strains of *Staph. aureus* studied in this work is that of the National Food and Drug Administration—the so-called F. D. A. Method (see Circular No. 198, U. S. Dept. of

* Scientific Section, A. PH. A., Dallas meeting, 1937.

[1] University of Illinois, College of Pharmacy.

Agriculture, 1931) and this method was strictly adhered to throughout this work. A certain phenol resistance is set as the standard by the F. D. A. Method to be attained by the culture of *Staph. aureus* used in the test.

The oral strains of *Staph. aureus* used in this work were obtained by swabbing the gum-line, lips or tongue with a sterile swab dipped in sterile normal saline solution, then rubbing the swab over a glycerin agar plate and incubating 48 hours. The typical *aureus* colony was picked off and restreaked on another agar plate. An agar streak was then made from a colony on the second plate, after which the organism was put through sugar reactions to assure its identity.

EXPERIMENTAL WORK.

Fourteen strains of *Staph. aureus* obtained from the oral cavity were studied as well as five strains which may be considered as standard stock strains.

Ten of the oral strains were obtained from apparently healthy mouths (absence of apparent or known pathology) and the other four oral strains were obtained from cases of known pathology—a root canal infection, pyorrhea pocket and an inflammatory condition of the gum, and the fourth from infected tonsils in a severe case of sore throat.

All of the freshly isolated oral strains were studied as to reaction in carbohydrate media using the sugars considered significant for *Staph. aureus* according to "Bergey's Manual of Determinative Bacteriology," namely, dextrose, lactose, sucrose, mannitol, salicin, raffinose and inulin. The results were as follows:

CHART I.

Strain.	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	A.	B.	C.	D.
Dextrose	A	A	A	A	A	A	A	A	A	A	A	A	A	A
Sucrose	A	A	A	A	A	A	A	A	A	A	A	A	A	A
Lactose	A	A	A	A	A	A	A	A	A	A	A	A	A	A
Mannitol	A	A	O	A	O	A	A	A	A	A	O	A	A	A
Raffinose	O	O	O	O	O	O	O	O	O	O	O	O	O	O
Salicin	O	O	O	O	O	O	O	O	O	O	O	A	O	O
Inulin	O	O	O	O	O	O	O	O	O	O	O	O	O	O

A indicates an acid reaction; O indicates no reaction—neutral.

It is to be noted that three strains did not produce an acid reaction in mannitol while one strain produced acid in salicin medium.

All strains were studied as to litmus milk reaction. All but one (Strain 4) gave the characteristic acid and coagulation reaction in from 24 hours to 20 days. The exception gave an alkaline reaction and showed no coagulation.

Hemolysis on blood plates was shown by all strains but one (Strain 10).

The color of the agar streak growth varied from a faint, pale yellow to a rich orange.

Each of these fourteen strains was tested for its resistance to phenol. Only one strain, namely No. 6, met the F. D. A. standard; the others all fell short of this standard. The ten strains obtained from healthy mouths are numbered 1 to 10 and the four strains from pathological mouths are lettered A, B, C and D.

The standard required by the F. D. A. is as follows:

Phenol.	5 Min.	10 Min.	15 Min.	Or.	5 Min.	10 Min.	15 Min.
1-80	+	−	−		+	−	−
1-90	+	+	−		+	+	+

The results obtained from the fourteen freshly isolated strains of *Staph. aureus* are as follows:

CHART II.

Phenol.	5 Min.	10 Min.	15 Min.	Phenol.	5 Min.	10 Min.	15 Min.
Strain 1:				Strain 8:			
1-80	−	−	−	1-80	−	−	−
1-90	−	−	−	1-90	+	−	−
1-100	−	−	−	1-100	+	+	−
Strain 2:				Strain 9:			
1-80	−	−	−	1-80	−	−	+
1-90	−	−	−	1-90	−	−	−
1-100	+	−	−	1-100	+	−	−
Strain 3:				Strain 10:			
1-80	−	−	−	1-80	−	−	−
1-90	−	−	−	1-90	+	−	−
1-100	+	−	−	1-100	+	−	−
Strain 4:				Strain A:			
1-80	−	−	−	1-80	−	−	−
1-90	−	−	−	1-90	−	−	−
1-100	+	−	−	1-100	−	−	−
Strain 5:				Strain B:			
1-80	−	−	−	1-80	−	−	−
1-90	+	−	−	1-90	+	+	−
1-100	+	+	+	1-100	+	+	+
Strain 6:				Strain C:			
1-80	+	−	−	1-80	−	−	−
1-90	+	+	−	1-90	−	−	−
1-100	+	+	+	1-100	+	−	−
Strain 7:				Strain D:			
1-80	−	−	−	1-80	−	−	−
1-90	+	−	−	1-90	−	−	−
1-100	+	+	−	1-100	+	+	−

Of the 5 stock strains studied, four were purchased from the John McCormick Institute and are part of the American Type Culture Collection. These are:

1. *Staph. aureus* No. 152, from the Hygienic Laboratories at Washington.
2. *Staph. aureus* No. 4691, from G. F. Reddish—the standard organism used for work on disinfectants.
3. *Staph. aureus* No. 4776, from U. S. Hygienic Laboratory where it is used to test disinfectants.
4. *Staph. aureus*, Cordell strain.
5. *Staph. aureus*, A-209, was sent by Dr. G. F. Reddish as an especially good strain for antiseptic testing by the F. D. A. method.

The four stock strains or so-called "standard cultures" from the American Type Culture Collection were tested by the F. D. A. method five times each and strain A-209 was tested eleven times. The detailed results are shown in Chart III. It is interesting to note that these five strains met the F. D. A. standard in a widely varying degree which may be summarized as follows:

No. 152 in 0.0 per cent of the tests
No. 4691 in 20.0 per cent of the tests[1]
Cordell in 20.0 per cent of the tests[1]
A-209 in 36.0 per cent of the tests[2]
No. 4776 in 60.0 per cent of the tests.[3]

[1] In 4 tests it failed to survive the 1-80 for 5 min.

[2] In 2 tests it failed to survive the 1 in 80 for 5 min., but in 3 tests it survived the 1 in 80 for 10 min. In 3 tests it failed to survive the 1 in 90 for 10 min.

[3] In 1 test it failed to survive the 1 in 80 for 5 min. and in 1 test it survived the 1 in 80 for 10 min.

The N. F. VI standard, namely, that the organism is to be of such resistance as to be killed by 1–80 phenol in 10 minutes but survive 1–90 phenol for 10 minutes, is met by these same 5 strains as summarized below:

No. 152 in 40.0 per cent of the tests
No. 4691 in 80.0 per cent of the tests
Cordell in 80.0 per cent of the tests
No. 4776 in 80.0 per cent of the tests
A-209 in 45.0 per cent of the tests.

Of the fourteen oral strains, two meet the N. F. VI standards as compared with one meeting the F. D. A. standards.

CHART III.

Phenol.	5 Min.	10 Min.	15 Min.
Strain 152:			
1–80	−	−	−
1–90	−	−	−
1–80	−	−	−
1–90	−	−	−
1–80	−	−	−
1–90	+	+	−
1–80	−	−	−
1–90	−	−	−
1–80	−	−	−
1–90	+	+	−
Strain 4776:			
1–80	−	−	−
1–90	+	+	−
1–80	+	−	−
1–90	+	+	+
1–80	+	−	−
1–90	+	+	−
1–80	+	−	−
1–90	+	+	+
1–80	+	+	−
1–90	+	+	+
Strain-Cordell:			
1–80	−	+	−
1–90	+	+	−
1–80	+	−	−
1–90	+	+	+
1–80	−	−	−
1–90	+	+	−
1–80	−	−	−
1–90	+	+	−
1–80	−	−	−
1–90	+	−	+

Phenol.	5 Min.	10 Min.	15 Min.
Strain 4691:			
1–80	−	−	−
1–90	+	−	−
1–80	+	−	−
1–90	+	+	−
1–80	−	−	−
1–90	+	+	+
1–80	−	−	−
1–90	+	+	−
1–80	−	−	−
1–90	+	+	−
Strain A-209:			
1–80	+	−	−
1–90	+	−	−
1–80	−	−	−
1–90	+	−	−
1–80	−	−	−
1–90	+	+	+
1–80	+	−	−
1–90	+	+	−
1–80	+	−	−
1–90	+	−	−
1–80	−	+	−
1–90	+	+	−
1–80	+	−	−
1–90	+	+	+
1–80	+	−	−
1–90	+	+	+
1–80	+	+	−
1–90	+	+	+
1–80	+	+	−
1–90	+	+	−

A PHARMACOLOGICAL STUDY OF PHYTOLACCA.*

BY DAVID I. MACHT.[1]

INTRODUCTION.

The poke weed is a very common perennial plant in central and eastern North America, and indeed the largest herb known there. In the Southern States it frequently grows as high as 10 or 12 feet and nearly as broad. The purplish green stem is often several inches in diameter. The very long, thick and fleshy root resembles that of the horseradish and has therefore been the cause of numerous poisoning accidents, particularly since it has an acrid taste deceiving those unfamiliar with it. Europeans use the purple juice of the berries extensively for coloring their wines. Acids are employed to brighten this color, which changes to bottle green on addition of alkalis. The older generation of physicians used this perennial American plant as a medicine. It was official in the U. S. P., 1880 and 1890, and although no longer in the pharmacopœia is still described at the present time in the National Formulary and various dispensatories.

Preparations of both root and fruit of *Phytolacca* have been used therapeutically but the products of *Phytolacca radix* are considered more efficient. In the National Dispensatory the constituents of poke root are described as follows:

"The chemical composition of poke root is very peculiar. Its important active and poisonous constituent is an amorphous, bitter and acrid substance very similar to, if not identical with, saponin. This is probably the glucoside reported by Coscera. The alkaloid phytolaccin exists in very small amount. It occurs in white crystals, soluble in alcohol and somewhat in water, nearly insoluble in ether and chloroform. *Phytolaccic acid* is amorphous, soluble in water and alcohol, reduces silver salts and yields with earths and alkalis soluble salts, from which boiling hydrochloric acid separates the acid as a jelly. Sugars exist to the extent of nearly 10 per cent, and of starch there is an equal or greater amount. A little free formic acid, besides nearly 2 per cent of potassium formate, was obtained by Frankforter, as well as 6.2 per cent of calcium oxalate. The same chemist found more than 13 per cent of ash, nearly half of which was potassium oxide. The important constituent of the fruit, aside from the coloring matter, is phytolaccic acid. Various fruit-acids occur. The coloring matter is soluble in water, but not in alcohol, ether or chloroform. Phytolaccin is a tannin-like substance. The ash amounts to 8 or 10 per cent. The poisonous constituents of the fruit are apparently confined almost, if not wholly, to the seed."

The uses for which the dispensatories advocate this drug form a fantastic conglomeration of empirical indications impressing the modern pharmacologist as a complete reversion to the therapeutics of the Dark Ages. We read that the drug has been recommended as an emetic, purgative, a narcotic and a gargle and as a remedy for chronic rheumatism, granular conjunctivitis, ringworm and parasitic infections of the scalp and other skin diseases and for syphilis and cancer.

The writer has been unable to discover reports of any experimental pharmacological work on this subject. The only recent publication regarding poke root that he has found is an article of merely empirical and clinical character, entitled, "Poke Root in Medicine," by U. Aylmer Coates (*Am. J. Pharm.*, 93, 232 (1921)). Since our dispensatories, formularies and even pharmacopœias are still

* Scientific Section, A. PH. A., Washington, D. C., meeting, 1934.

[1] Pharmacological Research Laboratory, Hynson, Westcott & Dunning, Inc., Baltimore, Md.

cluttered up with numbers of useless and often dangerous vegetable drugs, it was obviously worth while for the writer to make a study of phytolacca preparations to determine whether or not they exert any or all of the interesting pharmacological effects attributed to them. The fluidextract of poke root and fluidextract of poke berries (the former containing 40 per cent and the latter 26 per cent alcohol) were employed as a starting-point. In some experiments, the fluidextracts were administered as such. In others, as, for instance, in studies on isolated tissues, the alcohol was evaporated on the water-bath and the residue taken up in physiological saline to make up the original volume. Experiments were made on living plants, living animals and animal tissues.

Phytopharmacological tests, made according to methods described elsewhere by the author (1), were performed on seedlings of *Lupinus albus*, large variety, grown in physiological saline. The fluidextract as such was used in 1.0 and 0.5 per cent solutions and compared with control saline solutions containing, respectively, 0.5 and 1.0 per cent of 95 per cent alcohol. Even the dilute concentrations employed were markedly toxic for plant protoplasm. Seedlings grown in 1.0 per cent solutions gave a reading of 37 per cent while those grown in 0.5 per cent solutions yielded a phytotoxic index of 43 per cent.

When tested on animals and animal tissues, evaporated saline suspensions of *Phytolacca* were found to be very irritating. A drop or two instilled into the eyes of a rabbit produced marked reddening and irritation of the conjunctivæ. Similarly, one cc. of saline suspension, injected subcutaneously in rabbits and other animals, produced local infiltration and signs of painful irritation.

The toxicity of the saline suspensions was tested on goldfish, mice, rats, guinea pigs, rabbits and cats. Goldfish placed in water containing 1.0 per cent solution of fluidextract of *Phytolacca* in water keeled over on the side in 27 minutes. Arrest of respiration and death of goldfish occurred 40 minutes after their immersion in such solutions. Mice, intraperitoneally injected with as little as 0.25 cc. of such saline suspensions, died within a few minutes. The lethal intraperitoneal dose for medium-sized rats, weighing from 150 to 200 Gm., was one cc. The toxicity of such solutions was about the same for guinea pigs as it was for rats, computed on the basis of their relative weights.

Inasmuch as poke root has been recommended as a slowly acting emetic, cats were used in another series of experiments to investigate this particular effect ascribed to the drug. Administration by stomach tube of from 5 to 10 cc. of fluidextract of poke root diluted with water, was succeeded by repeated retching and violent vomiting, followed by prostration. This emesis was evidently not the result of any specific action on the vomiting center but rather a consequence of the gastro-intestinal irritation effected by the drug.

To ascertain whether any really narcotic action could be effected by small doses of the saline suspensions of the evaporated poke root extract, the writer made an experimental psychological study in which he employed methods described elsewhere (2). White rats, previously trained to run in the circular maze, were injected with small, non-toxic doses of 0.1 to 0.25 cc. of the suspensions and their subsequent behavior in the maze was carefully studied. No difference was noted in the rats' running time, the number of errors made and much less in their neuromuscular apparatus.

Studies were then made to determine whether or not poke root preparations are laxatives in the therapeutic sense of the word. Experiments were made on isolated intestinal loops from cats and rabbits kept alive in oxygenated Locke solution at body temperature. It was found that addition of saline suspension of poke root to the bath in which the intestinal preparation had been suspended produced no stimulation at all of the rhythmic peristaltic contractions. On the contrary, such saline suspensions of *Phytolacca* extract paralyzed the intestinal preparations. Occasionally this real paralysis of the smooth muscle was preceded by increased contraction due to irritating action of the drug. The paralysis of the tissue was proven by its failure to respond, after treatment with poke root or poke berry suspensions, to such specific stimulants of the intestine as pilocarpine, physostigmine or even barium chloride.

Fig. 1.—Small intestine of cat showing normal rhythmic contractions on very slowly moving drum. Powerful stimulation by 5 mg. of pilocarpine. Paralysis by 5 cc. of evaporated poke root extract in saline. Second dose of pilocarpine producing no response, indicates death of preparation.

In order to investigate the alleged laxative effect of *Phytolacca* extracts, the writer made another series of experiments on rats with emulsions of finely divided charcoal with and without the drug by a method described in detail elsewhere (3). Such tests revealed no difference between the controls and those rats which had been given *Phytolacca* emulsions in small quantities.

Inasmuch as empirical clinicians advocate the use of this drug in the treatment of chronic rheumatism, the writer deemed it worth while to investigate the possible antipyretic action of *Phytolacca*. Arthritis cannot be experimentally produced in animals. Even if it could be produced, it is practically impossible to study the effects of various analgesics on that type of pain in lower animals. It has been found, however, that antirheumatic drugs generally exert also an antipyretic action. Accordingly, fever was produced by injecting hay infusion in several rabbits. Before administration by stomach tube of a dose of *Phytolacca* extract and at various intervals thereafter the temperature of the rabbits was carefully measured. It was found that no antipyretic action was exerted by as much as 10 cc. of fluid evaporated extract of poke root in rabbits weighing 1.5 to 2 Kg. The following protocol serves as an illustration:

Gray rabbit weighing 2 Kg. 9:30 A.M., injected with 10 cc. of hay infusion. 12:00 M., temperature, 104° F.; 12:05 P.M., administered 10 cc. of evaporated extract of *Phytolacca*. 2:00 P.M., temperature, 104° F.; 3:00 P.M., temperature, 103° F.; 4:30 P.M., temperature, 103° F.

Control rabbit weighing 3 Kg. 9:35 A.M., injected with 10 cc. of hay infusion. 12:00 M., temperature, 104° F.; 2:00 P.M., temperature, 104° F.; 3:00 P.M., temperature, 103° F.; and 4:00 P.M., temperature, 103° F.

The effect of administration of one to ten cc. of saline suspension from the evaporated fluidextract of *Phytolacca* was studied on the kidney function of rabbits. The phenolsulphonphthalein renal test was employed in these experiments. Curiously enough, it was found that although the drug is irritant for the gastro-intestinal tract, even large doses of poke root or poke berry did not impair the kidney function.

Employing Rosenthal's bromsulphalein method (4), the writer also studied the effect of Phytolacca extracts on the liver function of rabbits. Five mg. of bromsulphalein per Kg. of rabbit were injected before administration of extracts and

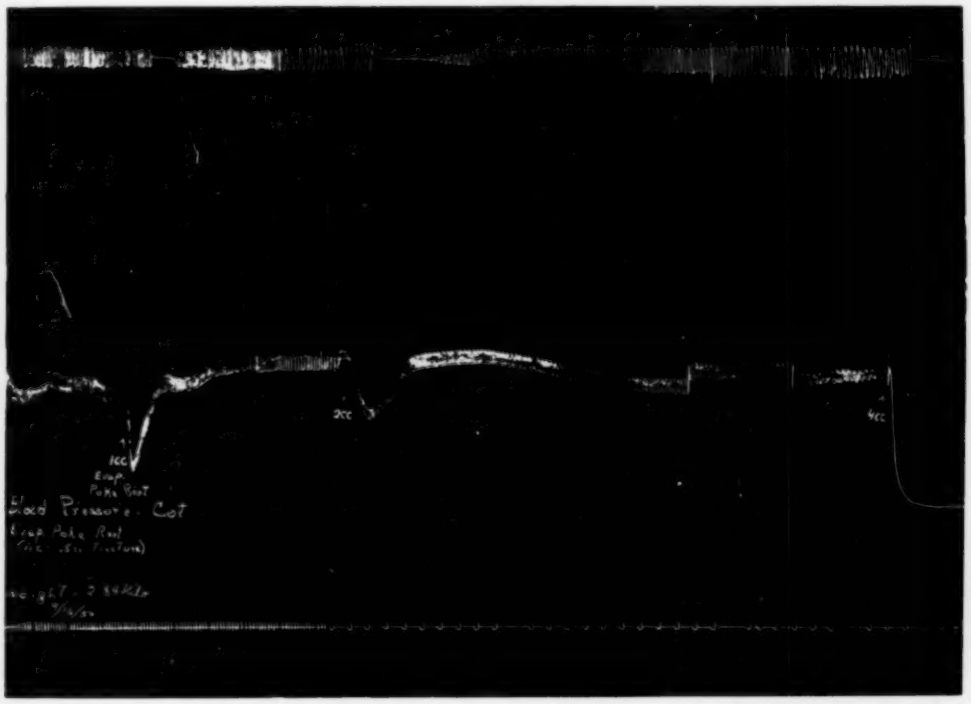


Fig. 2.—Blood pressure and respiratory curves of cat under ether anesthesia, showing effect of 1, 2 and 4 cc. of evaporated poke root extract injected intravenously.

after feeding the animal with the drug for periods ranging from one to three weeks, the liver function was tested again. Unlike the kidney function, the liver function was markedly impaired by *Phytolacca* feeding. The following protocols illustrate the effect of the drug on both kidney and liver function of rabbits:

RABBIT NO. 1, WEIGHING 2 KG.

Aug. 30	Kidney function test: phenolsulphonphthalein output in two hours (60% + 15%), 75%.
Sept. 6	Liver function test: bromsulphalein retention 15 minutes after injection, 5%.
Sept. 7	1 cc. of fluidextract of poke root, administered by mouth.
Sept. 8	1 cc. of fluidextract of poke root, administered by mouth.
Sept. 9	10 cc. of fluidextract of poke root, administered by mouth.
Sept. 13	Kidney function test: phenolsulphonphthalein output (75% + 10%), 85%.

Sept. 14 10 cc. of tincture of poke berry, administered by mouth.
Sept. 21 10 cc. of tincture of poke root, administered by mouth.
Sept. 22 Liver function test: bromsulphalein retention 15 minutes after injection, 10%.

RABBIT NO. 2, WEIGHING 2.5 KG.

Oct. 4 Kidney function test: phenolsulphonphthalein output in two hours, 80%.
Oct. 10 Liver function test: bromsulphalein retention 3 minutes after injection, 35%; 15 minutes after injection, 10%.
Oct. 13–25 Given fluidextract of *Phytolacca* in 5 cc. doses for ten days.
Oct. 27 Kidney function test: phenolsulphonphthalein output, 80%.
Oct. 28 Liver function test: bromsulphalein output 3 minutes after injection, 45%; 15 minutes after injection, 30%.

Finally, studies were made of the effect of *Phytolacca* solutions on circulation and respiration of cats under ether anesthesia. It was found that as little as 1.0 cc. of the evaporated fluidextract of the root, taken up in physiological saline and injected intravenously, markedly depressed the respiration and the circulation. Two cc. of the suspension paralyzed the respiration temporarily, and the animal slowly recovered. Four cc. simultaneously paralyzed both the heart and respiration.

COMMENT.

All the findings obtained in the experiments herein described are of particular interest when compared with the therapeutic claims for *Phytolacca* preparations found in the old textbooks and dispensatories. There is undoubtedly no rational basis for the employment of the drug in either syphilis or cancer or even in any other of the long list of ailments for which *Phytolacca* is recommended in those works. The drug is certainly a powerful irritant when administered locally and a violent poison when given internally in sufficiently large doses. It paralyzes the intestines and any purgative effect which may have been noted after its administration was doubtless but a manifestation of systemic poisoning. The vomiting produced by the drug is not the result of specific stimulation of the emetic center in the medulla but of intense irritation of the intestinal tract, as post-mortem examination of animals poisoned with large quantities of *Phytolacca* given by stomach tube has demonstrated. There is no experimental evidence to support the claims for its supposedly sedative or narcotic action on the neuromuscular system. Its vaunted tendency to reduce obesity may be ascribed to its general systemic poisoning of patients rather than to any specific action of the drug on the metabolism. *Phytolacca* has been recommended in the treatment of ringworm and other parasitic infections of the scalp, for which it may be effectively used, perhaps, but the writer is inclined to ascribe its action in such cases to the local irritation it produces and to the fact that it is a general protoplasmic poison. Poke root and poke berry preparations should therefore be considered as not only obsolete but dangerous.

SUMMARY.

1. A phytopharmacological study of extracts of *Phytolacca* was made on living plants and animals and on animal tissues.

2. The drug is very poisonous for seedlings of *Lupinus albus* grown in solutions of the respective extracts.

3. Small quantities of *Phytolacca* injected in rats trained in the circular maze produced no narcotic effect.

4. No antipyretic effect was noted after administration of the drug to rabbits.

5. The drug paralyzed smooth muscle preparations *in vitro* and had no truly laxative effect on the intestine *in vivo*.

6. Intravenous injection of saline suspensions of *Phytolacca* in cats produced marked depression and paralysis of both circulation and respiration.

7. These findings substantiate none of the claims made for the drug in the old textbooks.

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THE USE OF NEW SOLVENTS IN ALKALOIDAL ASSAYS.*

BY M. L. JACOBS [1] AND GLENN L. JENKINS.[2]

I. SOLUBILITIES AND DISTRIBUTION COEFFICIENTS OF CERTAIN ALKALOIDS IN ISOPROPYL ETHER AND METHYLENE CHLORIDE.[3]

SOLUBILITIES.

The solubilities of strychnine, quinine, atropine and caffeine in isopropyl ether, methylene chloride, mixtures of isopropyl ether-methylene chloride, mixtures of ethyl ether-chloroform, mixtures of isopropyl ether-chloroform and mixtures of ethyl ether-methylene chloride were determined.

The method employed for these determinations was as follows:

Twenty-five cc. of the solvent were placed in a small bottle and enough of the alkaloid added to insure an excess after shaking in a mechanical shaker over night. The bottle was then placed in a thermostat bath, regulated at 25° C. to 0.1°, and allowed to remain in the bath for at least twelve hours in order that equilibrium between the solute and solvent would be reached. A volume of about 5 cc. was then pipetted off, placed in a tared weighing bottle and its weight recorded. The solvent was allowed to evaporate spontaneously, the residue dried to constant weight at 100° C., cooled in a desiccator over sulfuric acid and its weight recorded.

The bottle was again shaken for three hours in a mechanical shaker and a sample determined as before. This procedure was repeated until constant results were obtained which was usually after the second shaking.

The calculations were made upon a basis of grams of alkaloid soluble in 100 Gm. of solvent at 25° C. and in the cases of chloroform and ether the solubilities of the various alkaloids were calculated from solubility data given in the United States Pharmacopœia, X.

The accompanying tables (Tables I, II, III and IV) show clearly the solubilities of the above-mentioned alkaloids in the individual solvents and mixed solvents under consideration.

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TABLE I.—STRYCHNINE.

Grams Soluble in 100-Gm. Solvent.

Ethyl ether	Ethyl ether, 3 vol. Chloroform, 1 vol.	Ethyl ether, 1 vol. Chloroform, 1 vol.	Ethyl ether, 1 vol. Chloroform, 3 vol.	Chloroform
0.021	1.62	3.26	6.27	13.5
Isopropyl ether	Isopropyl ether, 3 vol. Chloroform, 1 vol.	Isopropyl ether, 1 vol. Chloroform, 1 vol.	Isopropyl ether, 1 vol. Chloroform, 3 vol.	Chloroform
0.058	1.73	3.38	7.39	13.5
Isopropyl ether	Isopropyl ether, 3 vol. Methylene chlor., 1 vol.	Isopropyl ether, 1 vol. Methylene chlor., 1 vol.	Isopropyl ether, 1 vol. Methylene chlor., 3 vol.	Methylene Chloride
0.058	0.061	0.068	0.077	0.08
Ethyl ether	Ethyl ether, 3 vol. Methylene chlor., 1 vol.	Ethyl ether, 1 vol. Methylene chlor., 1 vol.	Ethyl ether, 1 vol. Methylene chlor., 3 vol.	Methylene Chloride
0.021	0.029	0.032	0.047	0.08

TABLE II.—QUININE.

Grams Soluble in 100-Gm. Solvent.

Ethyl ether	Ethyl ether, 3 vol. Chloroform, 1 vol.	Ethyl ether, 1 vol. Chloroform, 1 vol.	Ethyl ether, 1 vol. Chloroform, 3 vol.	Chloroform
74.00			44.31	61.7
Isopropyl ether	Isopropyl ether, 3 vol. Chloroform, 1 vol.	Isopropyl ether, 1 vol. Chloroform, 1 vol.	Isopropyl ether, 1 vol. Chloroform, 3 vol.	Chloroform
0.312			37.9	61.7
Ethyl ether	Ethyl ether, 3 vol. Methylene chlor., 1 vol.	Ethyl ether, 1 vol. Methylene chlor., 1 vol.	Ethyl ether, 1 vol. Methylene chlor., 3 vol.	Methylene Chloride
74.00			41.80	58.2
Isopropyl ether	Isopropyl ether, 3 vol. Methylene chlor., 1 vol.	Isopropyl ether, 1 vol. Methylene chlor., 1 vol.	Isopropyl ether, 1 vol. Methylene chlor., 3 vol.	Methylene Chloride
0.312			40.84	58.2

TABLE III.—CAFFEINE.

Grams Soluble in 100-Gm. Solvent.

Ethyl ether	Ethyl ether, 3 vol. Chloroform, 1 vol.	Ethyl ether, 1 vol. Chloroform, 1 vol.	Ethyl ether, 1 vol. Chloroform, 3 vol.	Chloroform
0.18	0.39	1.58	5.39	12.20
Isopropyl ether	Isopropyl ether, 3 vol. Chloroform, 1 vol.	Isopropyl ether, 1 vol. Chloroform, 1 vol.	Isopropyl ether, 1 vol. Chloroform, 3 vol.	Chloroform
0.15	0.30	1.39	5.29	12.20
Isopropyl ether	Isopropyl ether, 3 vol. Methylene chlor., 1 vol.	Isopropyl ether, 1 vol. Methylene chlor., 1 vol.	Isopropyl ether, 1 vol. Methylene chlor., 3 vol.	Methylene Chloride
0.15	0.29	1.27	4.50	8.67
Ethyl ether	Ethyl ether, 3 vol. Methylene chlor., 1 vol.	Ethyl ether, 1 vol. Methylene chlor., 1 vol.	Ethyl ether, 1 vol. Methylene chlor., 3 vol.	Methylene Chloride
0.18	0.26	1.97	4.72	8.67

TABLE IV.—ATROPINE.

Grams Soluble in 100-Gm. Solvent.

Ethyl ether	Ethyl ether, 3 vol. Chloroform, 1 vol.	Ethyl ether, 1 vol. Chloroform, 1 vol.	Ethyl ether, 1 vol. Chloroform, 3 vol.	Chloroform
5.63	12.14	28.50	52.50	67.56
Isopropyl ether	Isopropyl ether, 3 vol. Chloroform, 1 vol.	Isopropyl ether, 1 vol. Chloroform, 1 vol.	Isopropyl ether, 1 vol. Chloroform, 3 vol.	Chloroform
1.03	11.22	24.9	47.20	67.56
Ethyl ether	Ethyl ether, 3 vol. Methylene chlor., 1 vol.	Ethyl ether, 1 vol. Methylene chlor., 1 vol.	Ethyl ether, 1 vol. Methylene chlor., 3 vol.	Methylene Chloride
5.63	17.69	32.23	45.55	65.23
Isopropyl ether	Isopropyl ether, 3 vol. Methylene chlor., 1 vol.	Isopropyl ether, 1 vol. Methylene chlor., 1 vol.	Isopropyl ether, 1 vol. Methylene chlor., 3 vol.	Methylene Chloride
1.03	10.08	22.9	43.7	65.23

It will be observed upon examination of Table I that strychnine is more soluble in isopropyl ether than in ethyl ether, and a great deal more soluble in chloroform than in methylene chloride. The best solvent, then, for strychnine is chloroform and the best mixed solvent is a 3:1 mixture of isopropyl ether and chloroform.

Table II indicates that quinine is a great deal more soluble in ethyl ether than in isopropyl ether, while its solubility in methylene chloride is slightly less than in chloroform. Due to a gradual darkening and the formation of a viscid liquid in each case, it was very difficult to prepare saturated solutions of quinine in methylene chloride and in mixed solvents where methylene chloride was one of the components. It would appear, however, that quinine is not nearly as soluble in mixtures of ethyl ether-methylene chloride and isopropyl ether-methylene chloride as might be expected when its solubility in the individual solvents is considered. It is also of interest to note that quinine in the presence of methylene chloride gradually undergoes decomposition. Such a decomposition, however, would probably not interfere with the use of this solvent in the assay of cinchona, since the assay could be completed before any appreciable change took place. Experiments will be recorded later to substantiate or disprove this conclusion.

Table III shows that caffeine is soluble to the extent of 0.18 Gm. in 100 Gm. of ethyl ether and 0.15 Gm. in 100 Gm. of isopropyl ether. It also shows that caffeine is soluble in chloroform to the extent of 12.2 Gm. per 100 Gm. of solvent and in methylene chloride to the extent of 8.67 Gm. in 100 Gm. of solvent. In other words, isopropyl ether is practically as good a solvent as ethyl ether for caffeine, while methylene chloride dissolves only about two-thirds as much as chloroform.

In Table IV it may be seen that atropine is soluble in ethyl ether to the extent of 5.63 Gm. per 100 Gm. of solvent and in isopropyl ether to the extent of 1.03 Gm. per 100 Gm. of solvent. Its solubility in chloroform is 67.56 Gm. per 100 Gm. of solvent, and in methylene chloride 65.23 Gm. per 100 Gm. of solvent.

DISTRIBUTION COEFFICIENTS.

In 1914, Marden and Elliott (1) published a paper on the methods of extraction by means of immiscible solvents, in which they dealt mainly with distribution ratios of certain alkaloids between water and the immiscible solvents, chloroform and ether. These investigators pointed out that by use of the distribution coefficients, and a certain algebraic formula, the number of extractions necessary to remove practically all of a given alkaloid from aqueous solution could be calculated.

To calculate the distribution ratio (d) of the various alkaloids they used the following expression:

$$\frac{\text{Concentration in 10 cc. water}}{\text{Concentration in 10 cc. of non-aqueous solvent}} = \frac{C_1}{C_2} = (d)$$

and for the calculation of the number of shakings necessary for an extraction the following algebraic formula:

$$\frac{X_n}{X_o} = \left(\frac{da}{e + da}\right)^n$$

where

a = volume of aqueous solvent
e = volume of non-aqueous solvent

X_o = original amount of material in the aqueous layer to be extracted
X_n = amount of material in the water layer after n extractions.

The expression X_n/X_o = the fraction of material in the water layer after n extractions. Thus, it is seen that the smaller the value of X_n/X_o when calculated from the above formula, the fewer number of extractions necessary for complete removal of the alkaloid from aqueous solution.

In the aconitine, ether and aqueous ammoniacal system, using 100 cc. of water, 5 cc. of ammonia water and 50 cc. of ether, the result, (d) = 0.140 was obtained, and when 30 cc. of chloroform was used in place of the 50 cc. of ether the value of 0.017 (d = 0.017) was obtained. Thus, chloroform is shown to be a better immiscible solvent than ether for extracting aconitine from aqueous solution.

In the system atropine, water and chloroform the distribution ratio was found to be small, therefore, three extractions with 10-cc. portions of chloroform from 50 cc. of aqueous solution completely removed the atropine.

Codeine showed a high distribution ratio between water and ether (d = 0.939) and a low ratio between water and chloroform (d = 0.0067), indicating that chloroform is much the better immiscible solvent. Experiments showed this to be true.

The value of (d) for coniine between water and ether was shown to be about 0.05 and it was found that from three to five extractions, with 10-cc. portions of ether, would extract more than 99 per cent of this alkaloid. It was pointed out that due to the volatility of the coniine the partition ratio was hard to obtain.

The distribution ratio of quinine between water and chloroform was found to be very small. Thus, three washings with 10-cc. portions of chloroform almost completely removed the quinine.

The value of knowing the distribution ratio between immiscible solvents in alkaloidal assaying is apparent when one considers that from such knowledge the number of extractions necessary in any given case may be calculated. Therefore, the tedious process of testing for complete extraction by means of some alkaloidal reagent is eliminated. With this thought in mind it was decided to determine the distribution ratios of certain alkaloids in the systems water–isopropyl ether, water–methylene chloride, and also, between water and various mixtures of these immiscible solvents. With this data at hand it was thought that a more intelligent study of the use of these solvents in alkaloidal assaying could be made.

Accordingly, the distribution ratios of atropine, caffeine, quinine and strychnine between water and isopropyl ether, water and methylene chloride and water and mixtures of isopropyl ether-methylene chloride were determined.

In calculating the distribution ratios (d) the solubility of methylene chloride in water and the solubility of water in methylene chloride was considered to be negligible, therefore, the volume of each upon saturation with the other was taken as the initial volume. In the case of isopropyl ether and water the solubility of isopropyl ether in water was taken as 8 cc. in 100 cc. and of water in isopropyl ether as 2 cc. in 100 cc. at 25°+ C. These values are only approximately accurate, but are sufficiently close to the true values as not to make any appreciable difference.

The alkaloids used in the determinations were Merck and Company products. The isopropyl ether was obtained from the Carbide and Carbon Chemicals Corporation and conformed to the following specifications,

Boiling range	90 per cent distilled between 66° and 69° C. at 760-mm. pressure
Initial boiling point	Not less than 60° at 760-mm. pressure
Dry point	Not more than 70° at 760-mm. pressure
Color	Not more than 2% yellow
Specific gravity	0.723 to 0.729 at 20/20° C.
Residue	Not more than 0.1 per cent
Acidity	A 50-cc. sample does not contain more than the equivalent of 0.1 cc. normal acid or alkali
Suspended matter	Practically free from suspended matter

The product was subjected to careful distillation before use in order to get rid of the non-volatile residue. Only that portion distilling between 66°+ C. and 69°+ C. was used.

The methylene chloride used was obtained from the Advance Solvents and Chemical Corporation and E. I. duPont de Nemours and Company. The two products were essentially the same and conformed to the following specifications:

Color	Water white
Odor	No foreign odor
Boiling range	39.2° C. to 40° C. at 760 mm.
Specific gravity	1.33 at 15°/4° C.
Residue	None
Moisture	No cloud at −24° C.
Acidity	Less than 0.001 per cent calculated as HCl

These products were also subjected to careful distillation in order to get rid of any non-volatile residue.

The experiments were carried out in narrow glass-stoppered bottles in a constant temperature bath regulated at 25° C. to ± 0.1° The bottles were so arranged in the bath that they could be turned end over end at a rate of about 20 revolutions per minute. At the end of one hour the bottles were allowed to stand in the bath until the two layers were completely separated and clear, after which time 25 cc. of the non-aqueous solvent was pipetted off, the solvent allowed to evaporate spontaneously and the residue dried to constant weight in a desiccator over sulfuric acid. The alkaloids were determined gravimetrically.

The technique used is essentially the same as that used by Marden and Elliott (2), only differing in minor details, as to time, etc.

EXPERIMENTAL.

Strychnine.—The distribution coefficients of strychnine in the systems (*a*) water and isopropyl ether (*b*) water and a 3:1 mixture of isopropyl ether-methylene chloride, and (*c*) water and methylene chloride were determined. For these determinations 100 cc. of aqueous alkaloidal solution, 40 cc. of immiscible solvent and 5 cc. of ammonia water were used in each case. The results obtained are given in Table V.

TABLE V.—DISTRIBUTION RATIO OF STRYCHNINE BETWEEN WATER AND ISOPROPYL ETHER.

Wt. Strychnine in Sample.	Wt. Found in 25 Cc. Isopropyl Ether.	Wt. in Isopropyl Ether Layer 32 cc.	Wt. in Aqueous Layer 113 cc.	Concn. (d) in 10 Cc. H_2O / Conc. in 10 Cc. Non-Aqueous Solvent.
0.0103	0.0027	0.0035	0.0068	0.599
0.0123	0.0032	0.0041	0.0082	0.608
0.0166	0.0044	0.0056	0.0110	0.594
			Average	0.600

As may be seen from Table V, the value of (d) is 0.600. This means that 0.6 of the strychnine remains in the aqueous layer after one extraction, and upon extracting 50 cc. of the aqueous solution with 10-cc. portions of isopropyl ether (using 14 cc. for the first portion to allow for saturation of the aqueous layer) the value of (d) would be

$$\frac{0.6 \times 50}{0.6 \times 50 + 10} = \frac{30}{40} = 0.75$$

and it may be calculated that twelve such extractions $\left(\frac{1}{1.3}\right)^{12}$, would not remove much over 96.5 per cent of the alkaloid from aqueous solution, indicating that isopropyl ether is entirely unsatisfactory for this purpose. Calculations:

$$\left(\frac{1}{1.3}\right)^{12} = 30.00; \quad \frac{1 \times 100}{30} = 3.33\%; \quad 100.00 - 3.33 = 96.67\%$$

TABLE VI.—DISTRIBUTION RATIO OF STRYCHNINE BETWEEN WATER AND A 3:1 MIXTURE OF ISOPROPYL ETHER-METHYLENE CHLORIDE.

Wt. Strychnine in Sample.	Wt. Found in 25 Cc. Isopropyl Ether-Methylene Chloride, Layer.	Wt. in Isopropyl Ether Methylene Chloride (Layer 32 Cc.).	Wt. in Water (Layer 113 Cc.).	(d.)
0.0381	0.0214	0.0274	0.0107	0.110
0.0481	0.0231	0.0296	0.0111	0.107
0.0546	0.0263	0.0336	0.0125	0.106
			Average	0.107

It will be observed from Table VI (d = 0.107) that about one-tenth of the strychnine remains in the aqueous solution when equal volumes of the two solvents are used, and therefore, if 50 cc. of the aqueous solution of the alkaloid is extracted with 10-cc. portions of a 3:1 mixture of isopropyl ether-methylene chloride (14 cc. for the first portion to allow for saturation of the aqueous layer) the value of (d) becomes

$$\frac{0.107 \times 50}{0.107 \times 50 + 10} = \frac{5.35}{15.35} = 0.384$$

and it would require only four extractions $\left(\frac{1}{2.8}\right)^4$ to remove over 99 per cent of the strychnine and six extractions to almost completely remove the alkaloid from aqueous solution.

When it is remembered that the specific gravity of the immiscible solvent is an important factor in alkaloidal assay procedures, especially in extracting the alkaloid from aqueous solution, and that the specific gravity of a 3:1 mixture of isopropyl ether-methylene chloride is less than water, such a mixture should prove satisfactory in the assay of nux vomica.

TABLE VII.—DISTRIBUTION RATIO OF STRYCHNINE BETWEEN WATER AND METHYLENE CHLORIDE.

Wt. Strychnine.	Wt. Found in 25 Cc. Methylene Chloride.	Wt. in Methylene Chloride Layer (40 Cc.).	Wt. in Aqueous Layer (105 Cc.).	(*d*.)
0.0811	0.0493	0.0788	0.0023	0.010
0.1204	0.0733	0.1168	0.0036	0.011
			Average	0.0105

As may be seen in the case of water and methylene chloride the distribution ratio is 0.0105. Thus, when equal mixtures of these liquids are used a large per cent of the strychnine passes into the methylene chloride layer and when 50 cc. of the aqueous solution is extracted with 10-cc. portions of methylene chloride the value of (*d*) becomes

$$\frac{0.010 \times 50}{0.010 \times 50 + 10} = \frac{0.5}{10.5} = 0.048$$

and two extractions with 10-cc. portions $\left(\frac{1}{21}\right)^2$ will remove over 99.5 per cent of the strychnine from aqueous solution. This indicates very clearly that methylene chloride is satisfactory for this purpose.

To prove the conclusion that two 10-cc. portions of methylene chloride will extract practically all of the strychnine from aqueous solution, samples were prepared and extracted, using 1 cc. of ammonia water. The results are given in Table VIII.

TABLE VIII.

Wt. Strychnine.	Total Weight Found.	Percentage Found.
0.1000	0.0994	99.4
0.1000	0.0995	99.5
		Average 99.45

The extractions were carried out by uniformly shaking the separatory funnels for two minutes in each extraction and then allowing sufficient time for the separation of the two layers.

Brucine.—The amount of brucine extracted from aqueous solution with isopropyl ether is so small that it is difficult to obtain the correct distribution ratio. Check results were not obtained; however, it is clear from the results obtained that isopropyl ether would not be satisfactory for this purpose.

A 3:1 mixture of isopropyl ether-methylene chloride will extract more brucine from aqueous solution than isopropyl ether alone, but in this case also, the number of extractions required are too great for the solvent to have any practical value.

The distribution ratio of brucine between water and methylene chloride was found to be 0.098. This would indicate that brucine could be removed from aqueous solution by relatively few extractions using methylene chloride; however, more extractions would be required for brucine than for strychnine.

Atropine.—The distribution coefficients of atropine in the systems (*a*) water and isopropyl ether, (*b*) water and a 3:1 mixture of isopropyl ether and methylene chloride, and (*c*) water and methylene chloride are given in Tables IX, X and XI.

TABLE IX.—USING ISOPROPYL ETHER.

Wt. Atropine.	Wt. in 25 Cc. Isopropyl Ether.	Wt. in Isopropyl Ether Layer (32 Cc.).	Wt. in Aqueous Layer (113 Cc.).	(*d*.)
0.0284	0.0051	0.0062	0.0219	0.943
0.0401	0.0073	0.0093	0.0307	0.935
			Average	0.939

Using equal volumes of the solvent and water about as much atropine remains in the aqueous solution after one extraction as is extracted. Obviously, it would require too many extractions with this solvent to be of practical value.

TABLE X.—USING A 3:1 MIXTURE OF ISOPROPYL ETHER-METHYLENE CHLORIDE.

Wt. Atropine.	Wt. in 25 Cc. Immiscible Solvent.	Wt. in Immiscible Solvent Layer (32 Cc.).	Wt. in Aqueous Layer (133 Cc.).	(*d*.)
0.0821	0.0301	0.0409	0.0412	0.308
0.1004	0.0366	0.0498	0.0506	0.301
0.1164	0.0432	0.0587	0.0577	0.301
				Average 0.306

When a 3:1 mixture of isopropyl ether and methylene chloride is used the value of (*d*) is 0.306. It would require 10 extractions with 10-cc. portions of such a mixture to extract 96.5 per cent of the atropine from 50 cc. of aqueous solution. It is clear, therefore, that such a mixture would not be satisfactory for this purpose.

TABLE XI.—USING METHYLENE CHLORIDE.

Wt. Atropine.	Wt. in 25 Cc. Methylene Chloride.	Wt. in Methylene Chloride Layer (40 Cc.).	Wt. in Aqueous Layer (105 Cc.).	(*d*.)
0.0804	0.0397	0.0635	0.0169	0.101
0.1005	0.0484	0.0774	0.0220	0.109
0.1205	0.0584	0.0934	0.0261	0.107
				Average 0.106

As may be seen from Table XI ($d = 0.106$), methylene chloride is a much better immiscible solvent to extract atropine from aqueous solution than a 3:1 mixture of isopropyl ether-methylene chloride. Calculations show that five 10-cc. portions of methylene chloride will remove 99.5 per cent from aqueous solution, which is about the same amount as may be removed by five 10-cc. portions of chloroform. Thus, methylene chloride might be used as a satisfactory substitute for chloroform in extracting atropine from aqueous solution.

Quinine.—The distribution ratio of quinine in the systems (*a*) water and isopropyl ether, (*b*) water and methylene chloride and (*c*) water and a 3:1 mixture of isopropyl ether-methylene chloride is small in each case. Tables XII, XIII and XIV show the results obtained in the above cases.

TABLE XII.—DISTRIBUTION RATIO OF QUININE BETWEEN WATER AND ISOPROPYL ETHER.

Wt. Quinine.	Wt. in 25 Cc. Isopropyl Ether.	Wt. in Isopropyl Ether Layer (32 Cc.).	Wt. in Aqueous Layer (113 Cc.).	(*d*.)
0.0662	0.0390	0.0624	0.0038	0.024
0.1036	0.0609	0.0974	0.0062	0.026
				Average 0.025

Using the value ($d = 0.025$) calculations show that three washings with isopropyl ether would remove over 99.9 per cent of quinine from aqueous solution.

TABLE XIII.—DISTRIBUTION RATIO OF QUININE BETWEEN WATER AND A 3:1 MIXTURE OF ISOPROPYL ETHER-METHYLENE CHLORIDE.

Wt. Quinine.	Wt. in 25 Cc. Immiscible Solvent.	Wt. in Immiscible Solvent Layer (32 Cc.).	Wt. in Aqueous Layer (113 Cc.).	(*d*.)
0.0801	0.0462	0.0739	0.0062	0.033
0.0951	0.0534	0.0854	0.0097	0.043
0.1002	0.0585	0.0936	0.0066	0.031
				Average 0.035

A 3:1 mixture of isopropyl ether-methylene chloride would be satisfactory for extracting quinine from aqueous solution; however, based on the distribution ratio ($d = 0.035$) it is not quite as good as isopropyl ether alone.

TABLE XIV.—DISTRIBUTION RATIO OF QUININE BETWEEN WATER AND METHYLENE CHLORIDE.

Wt. Quinine.	Wt. in 25 Cc. Methylene Chloride.	Wt. in Methylene Chloride Layer (40 Cc.).	Wt. in Aqueous Layer (105 Cc.).	(d.)
0.1014	0.0628	0.1004	0.0010	0.0039
0.1200	0.0743	0.1188	0.0012	0.0041
				Average 0.004

Thus, it may be seen that methylene chloride is exceedingly efficient as an immiscible solvent for extracting quinine from aqueous solution. Two 10-cc. portions will almost completely extract the quinine from 50 cc. of aqueous solution. Where the value of (d) is so small as in the above case the solubility of methylene chloride in water and water in methylene chloride should be taken into consideration. These values could not be found in the literature, and therefore were not considered in calculating the distribution ratios.

Caffeine.—The distribution ratios of caffeine in the systems (*a*) water and isopropyl ether (*b*) water and methylene chloride and (*c*) water and a 3:1 mixture of isopropyl ether-methylene chloride indicate that any of the three solvents could be used for extracting caffeine from aqueous solution. For some reason good results could not be obtained; however, sufficiently accurate data were obtained to justify the conclusion that a 3:1 mixture of isopropyl ether-methylene chloride or methylene chloride alone would be highly satisfactory for this purpose.

From a consideration of the physical properties, isopropyl ether and methylene chloride appear to be well suited for use in alkaloidal assay work. Isopropyl ether has a specific gravity of 0.723–0.729 at 20° C., and a boiling point of about 67° C. Methylene chloride has a specific gravity of 1.33 at 15° C. and a boiling point of about 40° C. By using a 3:1 mixture of isopropyl ether and methylene chloride, therefore, a solvent is obtained which has a specific gravity less than water. Such a condition is desirable when one wishes to extract an alkaloid from the immiscible solvent by use of acidulated water. On the other hand, if it is desired that the alkaloid be removed from aqueous solution methylene chloride alone is to be preferred, because it will constitute the bottom layer and thus may be drawn off from the aqueous layer in the separatory funnel.

CONCLUSIONS.

1. The solubilities of atropine, caffeine, quinine and strychnine in isopropyl ether, methylene chloride and mixtures of these solvents have been determined.

2. From a consideration of these solubilities, isopropyl ether and methylene chloride should prove to be valuable solvents in the quantitative estimation of alkaloids.

3. The distribution coefficients of atropine quinine and strychnine in the systems (*a*) water and isopropyl ether, (*b*) water and methylene chloride, and (*c*) water and a 3:1 mixture of isopropyl ether-methylene chloride have been determined.

4. The conclusion is reached from a study of the distribution coefficients that these solvents possess definite possibilities as immiscible solvents to be used in extracting certain alkaloids from aqueous solution.

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STUDIES ON CALCIUM CREOSOTATE. I. CHEMICAL OBSERVATIONS ON THE WATER-SOLUBLE CONSTITUENTS.*[1]

BY EDWIN J. FELLOWS.

According to Gordonoff (1) creosote is more extensively used than any other therapeutic agent in the treatment of pulmonary disorders. The oral administration of creosote is attended with numerous objections the most pronounced of which, even after small doses, is its tendency to produce nausea and vomiting. Various attempts have been made to overcome these objectionable features of creosote therapy by diverse modifications of creosote and its constituents.

Calcium creosotate, prepared by the interaction of equal parts of calcium oxide and creosote, is a dark brown powder of empyreumatic odor and phenolic taste, which has enjoyed extensive clinical use as a creosote substitute for a period of more than twenty years. In view of the fact that a search of the literature discloses an almost complete lack of information on this drug and particularly since it has been admitted to U. S. P. XI, it would seem advisable to subject it to a thorough investigation.

The U. S. P. states that calcium creosotate is a mixture of the calcium compounds of creosote. When equal parts of calcium oxide and creosote are allowed to interact, the mixture attains a rather high temperature. This would lead one to suspect that the original creosote might be somewhat altered in the course of preparation of calcium creosotate. It would therefore seem important to determine whether or not calcium creosotate approximates creosote chemically.

All attempts to extract calcium creosotate with organic solvents were unsuccessful. When extracted with water a small percentage of the calcium creosotate goes into solution; the major portion of the drug, however, is water insoluble. Since aqueous solutions of calcium creosotate are to be used in certain future experiments the present investigation has been limited to a study of the chemical nature of the water-soluble constituents of the drug. An aqueous solution of calcium creosotate which would contain a definite amount of the powdered drug would be desirable. Since this is impossible solubility experiments were carried out in an attempt to establish a relationship between the amount of water-soluble constituents and

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[1] The expense of this investigation was defrayed, in large part, by a grant from The Maltbie Chemical Co., Newark, New Jersey.

calcium creosotate powder. Various sized samples of calcium creosotate were extracted with distilled water and the calcium and phenolic content of the aqueous extracts determined.

Solutions of the water-soluble bodies of calcium creosotate have been hydrolyzed and the phenols removed and distilled in an effort to determine whether they approximate chemically, the phenolic bodies of creosote. In addition to reviewing the literature on the chemistry of creosote, Sickman and Fischelis (2) have advanced data to show that most official creosote samples have methoxyl numbers which are more or less within a definite range. In the present paper the hydrolyzed water-soluble phenols of calcium creosotate have been compared with the phenols of their precursor creosote using methoxyl numbers and the U. S. P. X specifications for creosote as comparative criteria.

If calcium oxide and creosote are allowed to interact *in the presence of water* "calcium creosotate solution" is obtained and this is of much greater phenolic concentration than an aqueous solution prepared from calcium creosotate powder. The phenols obtained from a solution prepared from calcium creosotate powder and the phenolic bodies of "calcium creosotate solution" have been compared with the phenols of creosote.

Experimental.—Samples of calcium creosotate powder ranging from 1.0 Gm. to 36.0 Gm. were placed in 240-cc. bottles, 200 cc. of carbon dioxide-free water added and shaken at a moderate rate on a shaking machine. As shown in Table I the 1- and 2-Gm. samples were not completely extracted after 6 hours shaking; however, at the end of 12 hours shaking these samples were completely extracted. When the residues from these samples were reëxtracted for 12 hours only traces of phenols were obtained. When the other samples were reëxtracted for twelve hours appreciable amounts of phenols could be obtained.

Using the method of J. Moir (3) all solutions were assayed for phenolic content by colorimetric comparison with a standard creosote solution. This method is based on the fact that phenols, except those in which the *p*-position is blocked, in the presence of a diazotized solution of *p*-nitraniline, will give a red color when made alkaline. The deep red color of the original calcium creosotate solutions did not introduce an error in the determinations because in the dilutions used the calcium creosotate solutions, before adding the diazo reagent, were practically colorless. Attempts were made to dilute the calcium creosotate solutions so that the phenolic content of the samples assayed would approximate the concentration of the standard which was 4.0 mg. of creosote per 100 cc.

Just before using, the *p*-nitraniline reagent (1.5 Gm. *p*-nitraniline, 40 cc. conc. HCl and 500 cc. distilled water) was cooled to 0° C. and sodium nitrite solution (20%) added until decolorization took place. Of each of the diluted calcium creosotate samples twenty-five cc. were placed in a 100-cc. volumetric flask containing 10.0 cc. of the diazotized *p*-nitraniline reagent, shaken and allowed to stand for several minutes. Seven cc. of NaOH solution (15.0%) were then added and the volume adjusted to 100 cc. with distilled water. A standard solution of creosote (2 mg. creosote in 1 cc.) was treated in the same manner as the calcium creosotate solutions and comparisons made in a colorimeter.

Total ash obtained by evaporation and incineration of 25.0-cc. portions of the solutions has been obtained from each sample of calcium creosotate powder and expressed as calcium oxide in Table I. This is permissible since preliminary tests had shown that oxalate precipitation values agreed in all respects with the total ash results. Discrepancies in the amounts of water-soluble phenols obtained from given amounts of the powdered drug prompted the determination of total organic matter present in the powdered drug. Calcium creosotate powder which had been dried to constant weight over sulfuric acid was completely incinerated, the residual calcium oxide weighed, and the loss in weight calculated as organic matter.

One hundred cc. of creosote of the same lot used in the preparation of calcium creosotate

powder and "calcium creosotate solution" were distilled and subjected to the analytical procedures shown in Table II.

Two and four-tenths Kg. of calcium creosotate powder were extracted with 16 liters of distilled water, the aqueous extract removed from the residual drug by filtration and the water-insoluble residue washed with four liters of distilled water. The filtrate and washings were acidified with concentrated HCl and subsequently extracted with ethyl ether. This extract was washed with distilled water until the washings showed no cloudiness upon the addition of silver nitrate. After allowing the extract to stand over anhydrous sodium sulfate for several days the ether was removed by distillation under reduced pressure, 100 cc. of the residue remaining in the flask distilled at atmospheric pressure according to Method II of the U. S. P. X and the boiling point range recorded. The per cent methoxyl and specific gravity of the distillate were also determined.

In order to approximate the calcium creosotate hydrolysis and extraction as nearly as possible a sample of the creosote from which the calcium creosotate was prepared was placed in aqueous solution, acidified with HCl and the phenols extracted and treated in the same manner as the hydrolyzed calcium creosotate phenols. The analytical procedure on the phenolic distillate was the same as that used on the hydrolyzed calcium creosotate phenols. Twelve liters of six months old "calcium creosotate solution" (creosote content 1.8%) were hydrolyzed and distilled and the distillate examined in the same manner as the original creosote and hydrolyzed water-soluble phenols from calcium creosotate powder.

RESULTS AND DISCUSSION.

In Fig. 1 the creosote and calcium oxide content per cc. of each solution in Table I have been plotted against grams of calcium creosotate powder extracted by 200 cc. of distilled water. It is to be observed that the calcium oxide content increases with increased phenolic concentration. It is also obvious that with increased phenolic concentration there is a relative decrease in calcium oxide content. In the smallest sample the calcium oxide content is greater than the phenolic content and in the next higher sample the two concentrations are equal. Thereafter the phenolic values are always higher than the calcium. It is obvious that the calcium oxide content *per se* of the solutions in Fig. 1 is always in excess of 1.4 mg. per cc., the approximate solubility of calcium hydroxide at 25° C.

TABLE I.—PHENOLIC AND CALCIUM CONTENT OF CALCIUM CREOSOTATE POWDER IN CARBON DIOXIDE FREE WATER. ROOM TEMPERATURE 25° C.

Calcium Creosotate per 200 Cc. Water. Grams.	Hours Shaken.	Creosote Extracted by 200 Cc. Dist. Water. Grams.	Creosote per Cc. of Solution. Mg.	Ca as CaO per Cc. of Solution. Mg.
1.0	6	0.202	1.01	..
"	12	0.274	1.37	1.83
2.0	6	0.446	2.23	..
"	12	0.536	2.68	2.68
4.0	6	0.704	3.52	..
"	12	0.704	3.52	2.80
6.0	6	0.850	4.25	..
"	12	0.850	4.25	3.48
8.0	12	0.960	4.80	3.71
12.0	12	1.152	5.76	4.00
16.0	12	1.400	7.00	4.21
20.0	12	1.538	7.69	4.45
24.0	12	1.798	8.99	4.86
30.0	12	1.828	9.14	5.01
36.0	12	1.826	9.13	4.94

If an arbitrary assignment of a number representing the average molecular weight of the phenols of creosote is made it is possible to roughly estimate the theoretical amount of calcium oxide necessary to combine with a given amount of creosote phenols. In a complex mixture such as creosote quantitative estimations of the constituent phenols become a difficult task. The nearest approach to a determination of the percentage composition of creosote is the work of Behal and Choay (4). Inspection of their results indicates that 124, the molecular weight of guaiacol, is a representative figure for the average molecular weight of the creosote phenols. The inaccuracies involved in this assignment are manifold, particularly so in view of the fact that evidence which will be presented later indicates that the phenols of calcium creosotate are not entirely comparable chemically with the

TABLE II.

Material Distilled.	Volume Distilled. Cc.	B. P. Range. °C.	Distillate Distilling above 200° C. Per Cent.	Residue. Cc.	Sp. Gr. 25° C.	MeO Per Cent.
Creosote	100	200–215	100	2	1.085	12.5
Phenols extracted from acid aqueous solution of creosote	100	195–215	70	2	1.085	12.1
Water-soluble phenols from calcium creosotate powder	100	192–215	45	3	1.060	8.5
Phenols from "calcium creosotate solution"	100	192–215	50	2	1.050	4.5
U. S. P. X requirements for creosote	..	200–220	90	..	Not less than 1.075	....
Sickman and Fischelis for typical creosote samples	..	....	..	..	....	10.88 to 16.3

creosote phenols. However, it is of assistance in visualizing the possible nature of the mixtures in Fig. 1. If calculations are made in this manner the *observed* calcium values shown in Table I and Fig. 1 are always in excess of the theoretical amount necessary to combine with the *observed* phenol concentration. Calculated on the basis of formation of diphenolic salts it can be shown that the *excess* calcium increases with increased phenolic concentration so that in the more concentrated solutions the *excess* calcium greatly exceeds the solubility of calcium hydroxide. If calculations are made to determine the amount of calcium necessary to form monophenolic salts the excess calcium is practically the same in all the solutions of low phenol concentration but as the saturation point of the solutions is approached the amount of excess calcium gradually becomes smaller. While the data are insufficient from which to draw conclusions concerning the nature of the phenolic compounds it does appear that the calcium creosotate phenols are in solution as their calcium salts in equilibrium with an inorganic calcium compound.

Reference to Table I discloses the fact that the phenolic saturation point of the solutions, approximately 0.9 per cent creosote, is reached at the 24.0-Gm. sample. An interesting fact is disclosed in this table concerning the amount of water-soluble phenols obtained from the 1- and 2-Gm. samples. Inasmuch as equal parts of

calcium oxide and creosote are used in the preparation of calcium creosotate one might expect fifty per cent of the drug to be made up of water-soluble phenols. From Table I it is evident that the amounts of water-soluble phenols are considerably below this figure. Determination of the total organic matter in calcium creosotate powder, disclosed the fact that 56 per cent of the powdered drug was made up of organic matter. This coupled with the low phenolic concentrations of the solutions in Table I leads one to suspect that part of the creosote phenols used in the preparation of calcium creosotate have been altered in some manner so that they are no longer water soluble.

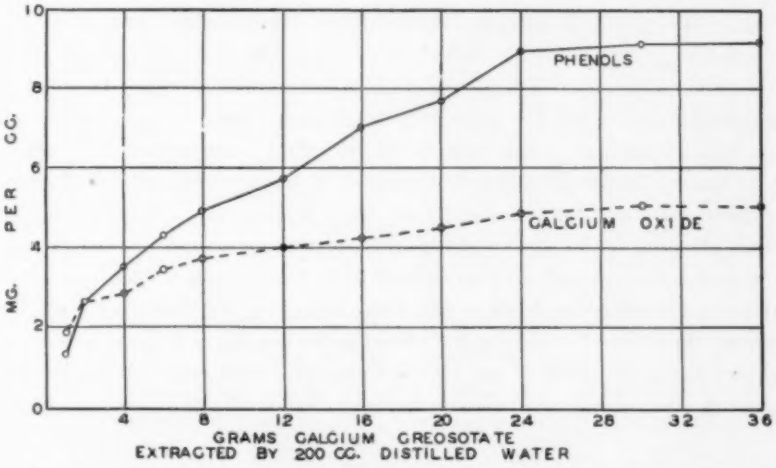

Fig. 1.—Samples of calcium creosotate powder which have been extracted by 200 cc. of distilled water are expressed in grams, and plotted against mg. creosote O————O and mg. calcium oxide O- - - - -O extracted during a 12-hour shaking period.

In Table II one finds that the creosote used in the preparation of the calcium creosotate examined in these experiments meets the U. S. P. X requirements. It is to be noted that the entire sample distils above 200° C. and the specific gravity of 1.085 is above the minimum of 1.075 required by the U. S. P. In addition to this the 12.5 per cent methoxyl is within the range found by Sickman and Fischelis for typical official creosote samples. However, it is to be noted that the phenols obtained from a sample of the same creosote after it had been placed in aqueous solution and acidified with HCl show some variations. The boiling point has been lowered and accordingly the amount which distils above 200° C. has been reduced. In contrast with the original creosote the boiling point range for these bodies is found to be 195–215° C. The U. S. P. X states that not less than 90 per cent of the creosote sample should distil above 200° C. With the volumes used, the entire sample of the original creosote distilled above 200° C., whereas only 70 per cent of the mixture obtained from the aqueous solution of creosote distilled above this temperature. On the other hand the specific gravity and the per cent methoxyl remain practically unchanged. The hydrolyzed water-soluble phenols of calcium creosotate powder show still greater variations. In addition to a lowered boiling point range and consequent diminution in the amount of material distilling above

200° C. the specific gravity requirement of not less than 1.075 is not attained by these bodies which have a specific gravity of only 1.060. The methoxyl per cent of 8.5 which is considerably below the value of 12.5 found for the original creosote indicates a lower guaiacol and creosol content. It may be suspected that if calcium salts of the phenols of creosote are formed in the preparation of calcium creosotate the methyl group of the methoxyl of part of the guaiacol and creosol might be replaced by calcium. Hydrolysis, then, would be productive of dihydroxy benzene and dihydroxy toluene compounds. However, if this does take place one would expect the boiling point of the mixture to be raised. Since guaiacol is very unstable in alkaline medium the true explanation of the decreased methoxy compound content probably lies in the alkalinity of the calcium creosotate. In any event, judging from the specific gravity and methoxyl data, the guaiacol or creosol, or guaiacol and creosol content of the hydrolyzed water-soluble phenols of calcium creosotate does not approximate that of the phenols of the original creosote. The hydrolyzed phenols obtained from "calcium creosotate solution" show essentially the same characteristics as those obtained by extraction of the powder with distilled water. The specific gravity and per cent methoxyl are even lower than the values found for the hydrolyzed phenols from the solution prepared from calcium creosotate powder. These lower specific gravity and methoxyl values appear logical if the alkalinity of the solution is a factor involved in the diminution of the methoxy compound content, because the phenolic bodies of "calcium creosotate solution" were exposed to the alkalinity for a period of 6 months as compared with a few days for the phenols obtained from the solution of calcium creosotate powder.

SUMMARY.

(1) The calcium and phenolic content of solutions obtained by water extraction of calcium creosotate power indicates that the phenolic bodies may be in solution as calcium salts in equilibrium with an inorganic calcium salt.

(2) Evidence is presented to show that portions of the original creosote phenols have been altered in some manner in the preparation of calcium creosotate so that they are no longer water soluble.

(3) The boiling point range of a phenolic mixture obtained by ethyl ether extraction of an aqueous solution of creosote acidified with HCl, was somewhat lower than that of the original creosote.

(4) Data are presented to show that the hydrolyzed water-soluble phenols of calcium creosotate are not entirely representative of the original creosote phenols. This variation is due to a diminution in the methoxy compound content of the water-soluble calcium creosotate phenols as compared with that of the original creosote phenols.

Grateful acknowledgment is hereby made to Dr. A. E. Livingston for the many helpful suggestions and encouragement given during the course of these experiments.

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AN IMMISCIBLE SOLVENT METHOD FOR THE DETERMINATION OF MORPHINE IN OPIUM.

BY E. DOWZARD, T. K. THOMAS AND M. RUSSO.*

During the past few years, a number of American and European chemists have suggested various methods for the determination of morphine in opium. The general opinion is that a desirable method should not involve the use of aliquot parts, and the morphine should be extracted with an immiscible solvent. The objection to the use of immiscible solvents is that owing to the insoluble nature of morphine in the solvents so far suggested, it has not been practicable to use more than about 1 Gm. of opium. Most American chemists consider that not less than 4 Gm. of opium should be used for the assay because of the lower experimental error.

After conducting a considerable number of experiments, we have finally developed a method which may prove reasonably satisfactory. The method is somewhat similar to an unpublished method by Eder and Wackerlin (1) with the exception that a different solvent is used and 4 Gm. of opium are taken for the assay. The solvent is a neutral mixture of 60 volumes of chloroform and 40 volumes of benzyl alcohol; 100 cc. of the mixture under the conditions of the assay will extract over 1 Gm. of morphine alkaloid. The details of the method are as follows:

Fig. 1.

Place 4 Gm. of opium which may be in the form of gum, powder or granules, in a 100-cc. porcelain mortar with a rough inner surface, add 8 to 12 cc. of distilled water and triturate with a rough pestle until a smooth paste is formed, free from discernible particles. This operation requires about 10 to 15 minutes. Add 2 Gm. of calcium hydroxide, 2 cc. of distilled water and continue triturating for about 5 minutes. A rubber policeman with one end sealed, should be used to scrape particles from pestle and sides of mortar during trituration. Then add three 10-cc. portions of distilled water, triturating for about 2 minutes, after each addition. Stir the mixture frequently during 10 minutes, then add 1 Gm. of wood flour,[1] which facilitates filtration. Mix well and allow to stand 5 minutes, stirring frequently.

Thorough trituration of the opium, even when in the form of powder is of great importance. Even with powder, low results are possible if the opium is merely shaken with the prescribed amount of water for 30 minutes and then with calcium hydroxide for 30 minutes before filtering.

The filtering apparatus consists of a short wide form 17G3, Jena fritted glass Büchner type filter funnel with a disc 65 mm. in diameter. The funnel is connected by means of a 32-mm. carbon filter tube to a 500-cc. separator, which is connected to a vacuum pump. The figure shows arrangement of the apparatus.

Before starting the filtration, place about 2 cc. of benzyl alcohol in the separator to prevent foaming during filtration. The mixture in the mortar is transferred to the filter, as much as possible of the residue left in the mortar being removed by means of the policeman. Suction is applied until all of the liquid has drained into the separator. The vacuum is broken and the mortar and pestle washed twice with two 8 cc. of lime water, using the policeman to remove particles. The combined washes are mixed thoroughly in the funnel with the residue for about 2 minutes by means of the policeman, a thin glass rod with one end drawn to a dull point may

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[1] The wood flour was obtained from Eimer & Amend, New York, N. Y.

be used to detach cake from the corner of the funnel. Suction is again applied until the liquid has drained into the separator. The mortar is then rinsed three times with 15 cc. of lime water. As before, each wash is thoroughly mixed with the residue in the funnel before applying suction.

The 5 washes are sufficient to remove all soluble and insoluble matter from the mortar and pestle. The residue in the funnel is now washed four times with 15 cc. of lime water each time. The suction is discontinued while each wash is thoroughly mixed with the residue. The filtrate may be slightly cloudy. The carbon filter tube and the inside of the lower portion of the funnel are rinsed with 5 cc. of distilled water. To the filtrate in the separator, add 75 cc. of solvent which is a neutral mixture of 60 volumes of chloroform and 40 volumes of benzyl alcohol.[1] Add 3 Gm. of ammonium chloride and shake vigorously for 2 minutes. Allow to separate for about 15 minutes. The solvent and the small quantity of emulsion is filtered through a small plug of absorbent cotton in a 32-mm. carbon filter tube into a 250-cc. separator. The last portion of the solvent is blown out by applying the mouth to end of filter tube. Wash the plug of absorbent cotton once with 5 cc. of solvent. Add 5 cc. of solvent to the alkaline liquid, shake gently for a few seconds. After about one minute, transfer solvent to the filter tube and repeat once. The solvent is blown out of the filter tube as before. The solvent in the 250-cc. separator is drawn into another 250-cc. separator, the small quantity of alkaline liquid is transferred to the 500-cc. separator containing the bulk.

Place 20 cc. of solvent in the empty 250-cc. separator, shake a few times, transfer to the 500-cc. separator, shake vigorously for 2 minutes, separate and repeat the routine twice. In all, the alkaline opium solution is extracted 4 times, once with 75 cc. and 3 times with 20 cc. of solvent. The solvent from each shake is filtered through the same plug of absorbent cotton that was used for the first shake. The solvent containing the alkaloids in the 250-cc. separator is now shaken for one and one-half minutes with a mixture of 3 cc. $N/1$ sodium hydroxide and 9 cc. of water, and allowed to separate for 20 minutes. The solvent is transferred to another 250-cc. separator, leaving the alkaline solution and any emulsion in the first separator. The solvent is shaken for one and one half minutes with 10 cc. of $N/10$ sodium hydroxide, allowed to separate and the solvent transferred to a third 250-cc. separator. The alkaline solution is added to the first alkaline extract in the first separator. 10 cc. $N/10$ sodium hydroxide is added to the empty second separator. After shaking a few times, the solution is added to the solvent in the third separator. The mixture is shaken for one and one-half minutes and the above routine repeated. The solvent is given two more shakes with 10 cc. of $N/10$ sodium hydroxide. In all, the solvent is shaken out 5 times, the last 4 times with 10 cc. $N/10$ sodium hydroxide. The sodium hydroxide solution of morphine is now shaken with 5 cc. of chloroform for a few seconds. The separated chloroform and the small quantity of emulsion is filtered through a fresh plug of absorbent cotton in a 32-mm. carbon filter tube and blown out. A second shake with 5 cc. of chloroform follows. The plug of absorbent cotton is then washed twice with a few cc. of distilled water; the chloroform is separated and the aqueous portion added to the sodium hydroxide solution of morphine, which is transferred to a tared 125-cc. Erlenmeyer flask and a few drops of methyl red indicator added. The chloroform is shaken with 5 cc. of distilled water and separated; the water is used to rinse out the separator which contained the sodium hydroxide solution of morphine. The separator is then rinsed out twice, each time with 5 cc. of $N/1$ sulfuric acid. Each wash is passed through the cotton plug in the filter tube, the filtrate passing into the Erlenmeyer flask containing the morphine solution.

The separator is again rinsed out with two 5-cc. portions of distilled water and the same routine followed. Sufficient $N/1$ sulfuric acid is then added to give a distinct acid reaction, usually 1 to 3 cc. will be required. If the solution is too dark to see the change in color, add a small piece of blue litmus paper. The flask containing the acidified solution is heated on a steam-bath with frequent shaking until the globule of chloroform has disappeared, the flask is then immersed in a steam-bath up to the neck and a stream of compressed air passed over the liquid until the solution weighs about 30 Gm. The solution is cooled, neutralized with 10% ammonia solution (about 1 drop will be required) and sufficient distilled water added to bring the weight up to 34 Gm. Add 2 cc. alcohol, 15 cc. ether, 0.6 cc. 10% ammonia solution and 0.5 Gm. ammonium

[1] Sufficient solvent for the assay is first shaken with 50 cc. of distilled water and sufficient ammonia to neutralize free acid.

sulfate, stopper the flask tightly and agitate without wetting the stopper until the morphine separates. Allow to stand over night at room temperature. The addition of ammonium sulfate induces rapid precipitation.

Remove the stopper and brush any adhering crystals back into the flask. Decant the ether layer through a 9-cm. filter paper and wash paper with 5 cc. of ether. Rinse the flask and contents with 15 cc. of ether. Pass the ether wash through the filter and again wash the filter with 5 cc. of ether. If necessary, wash the funnel tip with a few cc. of ether.

Pour the aqueous layer upon the filter without trying to remove all of the crystals from the flask. Wash the crystals in the flask and the contents of the filter with morphine-saturated water. Seven washes are given—5 cc. each time. Wash the crystals into the cone of filter with a few cc. of morphine-saturated water dropped from a pipette, followed by 2 cc. of distilled water. Place 5 cc. of methanol in the flask. Rotate the flask to detach the crystals from the sides and neck. Heat to the boiling point. Agitate to dissolve as much of the morphine as possible and pour the hot solution over the morphine on the filter, receiving the filtrate in a suitable flask. Repeat this treatment 13 times, using 5 cc. of methanol each time. A total of 70 cc. of methanol is used.

After the second or third wash, break up any clumps of alkaloid on the filter with a glass rod. After all visible morphine has been dissolved from the flask and filter, open the filter flap and drip the hot methanol over the edge of filter and on any morphine held in the flap. After the prescribed number of washes have been given, drip 5 cc. of cold methanol from a pipette on the outside tip of funnel to dissolve traces of morphine which may crystallize out from the methanol.

Cool the filtrate, add exactly 25 cc. of $N/10$ sulfuric acid and evaporate on a steam-bath to about 25 cc. Cool the liquid, dilute with 25 cc. of distilled water and titrate the excess acid with $N/10$ sodium hydroxide, using methyl red as the indicator. Each cc. of $N/10$ acid is equivalent to 0.02852 Gm. of anhydrous morphine alkaloid.

To 75 cc. of methanol, add 25 cc. of $N/10$ sulfuric acid. Evaporate on a steam-bath to about 25 cc. and titrate the excess acid with $N/10$ sodium hydroxide.

A correction for the acidity or alkalinity of the methanol is applied to the results obtained after titrating the morphine solution. The morphine obtained by this method is free from non-phenolic alkaloids. We have found that the morphine obtained by the U. S. P. XI method contains about 4% of non-phenolic alkaloids. Wallingford and Homeyer (2) have shown, that in addition to the non-phenolic alkaloids in the U. S. P. X assay morphine, there are other water-soluble basic substances, probably phenolic in character. So far, it has not been found practicable to remove these phenolic basic substances except by reprecipitation from water.

As the result of a few experiments, we have found that loss of morphine in the assay is to some extent counter-balanced by these water-soluble basic substances. Of course, with opium from various sources, these impurities will vary in quantity.

The following is a comparison of the results obtained by the U. S. P. XI and the new method. Powdered opium was used.

Morphine Alkaloid by U. S. P. XI Method.		Temperature during Precipitation.
Chemist A	11.27%	22.8°
	11.25	
		to
Chemist B	11.25	
	11.36	25° C.
Average	11.28%	

Morphine Alkaloid by New Method.		Temperature during Precipitation.
Chemist A	11.59%	23° to 26.5° C.
	11.63	23° to 25.5° C.
	11.68	19° to 25.5° C.
	11.68	17° to 27.0° C.
Chemist B	11.68	19° to 26.0° C.
Average	11.65%	

The morphine obtained by the U. S. P. XI method contains about 4% of non-phenolic alkaloids. If this correction is applied the results are as follows:

U. S. P. XI after Correcting for Non-phenolic Alkaloids.	New Method Free from Non-phenolic Alkaloids.
Morphine alkaloid	Morphine alkaloid
10.83%	11.65%

The following results were obtained with one sample of opium:

Morphine Alkaloid by U. S. P. XI Method.	Temperature during Precipitation.	Morphine Alkaloid by New Method.	Temperature during Precipitation.
13.59%	17° to 26° C.	14.19%	17° to 26° C.
Corrected for non-phenolic alkaloids			
13.05%	....	....	....

The results obtained by the new method were 0.38% to 0.6% higher than by the U. S. P. XI method. After correcting for the non-phenolic alkaloids the difference is 0.82% to 1.14%.

In all assays by the U. S. P. XI and the new method, the volume of methanol used was 75 cc.

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BROMOALKYL DERIVATIVES OF SALICYLIC ACID.*

BY E. MONESS AND W. G. CHRISTIANSEN.[1]

An unsaturated alkyl chain containing bromine has frequently been found of considerable value in producing a sedative effect in barbituric acid derivatives. Pernocton, for example, is secondary-butyl-β-bromoallyl barbituric acid. A combination of the sedative bromoalkyl group with the antipyretic and analgesic salicylic acid grouping offered interesting possibilities. We therefore prepared bromoallyl salicylate (I), and its acetyl derivative (II). The former was made by condensing sodium salicylate with 2,3-dibromopropene, and the latter by acetylating the condensation product. Biological tests revealed that both compounds were somewhat superior to acetyl salicylic acid in antipyretic activity, but were almost three times as toxic. The advantage of enhanced antipyretic action was therefore outweighed by increased toxicity.

Having in mind the preparation of α-bromoacrylyl salicylic acid we made three attempts at the preparation of intermediates:

(1) α-bromoacrylyl chloride from potassium α-bomoacrylate and thionyl chloride.

(2) α-bromoacrylyl chloride from potassium α-bromoacrylate and phosphorus oxychloride

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by the method used by Moureu (1) in the preparation of acrylyl chloride.

(3) α,β-dibromo-propionyl salicylic acid from salicylic acid and α,β-dibromo-propionyl chloride.

All three attempts were unsuccessful, yielding only resinous polymerization products.

EXPERIMENTAL.

Preparation of Bromoallyl Salicylate.—40 Gm. sodium salicylate (over 100% excess) which had been dried under a vacuum of 6–8 mm., and at a temperature of 170° C. for three hours, was placed in a flask with 25 Gm. dibromopropene and 45 cc. of acetone. The mixture was heated on the steam-bath, under reflux, for ten hours. After distilling off the acetone and unreacted dibromopropene, the oily residue was taken up in water and extracted with ether. This extract was washed with water, dilute sodium carbonate solution, and again with water, dried over anhydrous sodium sulfate and purified through charcoal. This gave a colorless ether solution. The ether was distilled off and the oil which remained was distilled *in vacuo*.

Yield—16 Gm. of a light yellow oil, b. p. 125–130° C./1–2 mm.
Molecular Weight: Found, 262; calculated for $C_{10}H_9O_3Br$, 257.

Preparation of Acetyl, Bromoallyl Salicylate.—6.9 Gm. bromoallyl salicylate was dissolved in 2.7 Gm. pyridine and cooled with an ice-salt mixture. Into this was stirred, drop by drop, over a period of thirty minutes, 2.7 Gm. of acetyl chloride. The liquid gradually turned into a semi-solid crystalline paste due to the formation of pyridine hydrochloride. The reaction mixture was then heated on the steam-bath for ten minutes and taken up in 150 cc. of ice water. The compound separated out as a dark brown oil, which was extracted with ether, and the extract dried and purified as before. The ether was then evaporated off, yielding a yellow oil which was dried *in vacuo* for two days at room temperature. There was not enough of it to warrant fractionation *in vacuo*, and a molecular weight determination was made without further treatment.

Molecular Weight: Found, 280; calculated, 299.

This low value is undoubtedly due to the presence of traces of solvent. The substance is otherwise pure. Ferric chloride produces no color. (The non-acetylated bromoallyl salicylate gives a deep purple with ferric chloride.) There is no unoccupied carboxyl as proved by the absence of acidity to phenolphthalein.

Attempted Preparation of α-Bromoacrylyl Chloride.—10 Gm. of the potassium salt of α-bromoacrylic acid (3) was refluxed on the steam-bath for two hours with a large excess of thionyl chloride. It was cooled, and diluted with dry ether, filtered from the white salt, and the ether distilled off. On distilling *in vacuo* an oil was obtained which was a mixture of thionyl chloride, and what was possibly α-bromoacrylyl chloride. When an attempt was made to fractionate this at atmospheric pressure, a few cc. of pure thionyl chloride came off, and then the distillation stopped. The substance in the flask proved nondistillable, becoming first viscous and then hard.

The same negative result was obtained when phosphorus oxychloride was used instead of thionyl chloride. Since α-bromoacrylic acid is known to be very un-

stable (2), it is not surprising to find the corresponding acid chloride extremely unstable.

Attempted Preparation of α,β-Dibromopropionyl Salicylic Acid.—5 Gm. salicylic acid was dissolved in 5 Gm. pyridine, and the solution cooled in an ice-salt bath. To this was added slowly, drop by drop, and with stirring, 11 Gm. of α,β-dibromo-propionyl chloride. A gummy mass soon formed, and it became impossible either to continue efficient stirring or to control the temperature. The mass was brown at first, but soon became purple. After all the acid chloride had been added the reaction mixture was heated on the steam-bath for five minutes. There was considerable foaming, accompanied by darkening of the reaction mixture. It was stirred into ice water, and a purple precipitate was obtained. It was isolated as a purple powder weighing 4 Gm. However, it was found to contain considerable water when heated on the steam-bath, and when completely dry was a semi-solid tarry substance. This on cooling solidified into a glassy substance which when powdered, was of a dark purple color. The powder was boiled with benzol, a large part remaining undissolved. The benzol solution was evaporated to dryness, leaving a brown glassy residue. On analysis this substance showed only a trace of bromine. Either the desired compound was not formed, or hydrolyzed in the attempt at purification.

The testing of the bromoalkyl salicylates for toxicity and antipyretic activity was done in the Biological Research Laboratories of E. R. Squibb & Sons and we gratefully acknowledge their assistance.

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A STUDY OF PRECIPITATION IN FLUIDEXTRACT OF UVA URSI I.*[1]

THE CRYSTALLINE NATURE OF THE PRECIPITATE IN FLUIDEXTRACT OF UVA URSI.

BY H. L. TISHER[2] AND C. O. LEE.[3]

INTRODUCTION.

Fluidextracts are a troublesome class of preparations because they precipitate badly upon standing. Years ago Lloyd said, "Physicians object to even muddy fluidextracts. Pharmacists feel annoyed and discouraged when they find their bottles partly filled with sediment, and this trouble (sediment) is the rule and not the exception"(3).

The causes for the formation of precipitates in fluidextracts are many, the chief of which is, perhaps, the fact that they are highly concentrated preparations. The subject has attracted many investigators.

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* Scientific Section, A. PH. A., Dallas meeting, 1936.

[1] An abstract of a thesis submitted to the faculty of Purdue University in partial fulfilment of the requirements for the degree of Master of Science by H. L. Tisher.

[2] J. K. Lilly Fellow, Purdue University, School of Pharmacy, 1930–1932.

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FLUIDEXTRACT OF UVA URSI.

The first formula for Fluidextract of Uva Ursi is credited to Maisch (2). His formula, with slight modification, was adopted by the U. S. Pharmacopœia of 1860. It has been retained in the succeeding revisions of the Pharmacopœia, except the last, with slight changes in formulas from time to time. Scoville (5) found that the preparation precipitated badly and in so doing showed a marked loss in astringency. He suggested that tannin-bearing preparations, such as fluidextracts, should be strongly alcoholic.

Fluidextract of Uva Ursi continues to precipitate over long periods of time. For this reason it is among the most troublesome of the fluidextracts; it is not unlikely that this is due to the large amount of tannin in Uva Ursi.

EXPERIMENTAL.

Two lots of Uva Ursi leaves, numbered 21839 and 97169, were furnished by the Eli Lilly Company, Indianapolis. These conformed to the official tests for identity and purity, and were used to prepare the many samples of the fluidextracts which are being reported upon in this study.

Plate I.

Plate II.

A STUDY OF THE p_H CHANGE IN FLUIDEXTRACT OF UVA URSI.

An official fluidextract was made from uva ursi, Lot 21839. By means of a Leeds and Northrup student potentiometer the p_H of the fluidextract was taken at irregular intervals for about eight months. The changes in p_H were not significant, leading us to conclude that the product which we had observed was a rather stable one in so far as any marked chemical changes were concerned.

CRYSTALLINE CHARACTER OF THE SEDIMENT IN FLUIDEXTRACT OF UVA URSI.

After studying many samples of the fluidextract it was observed that a precipitate occurred regularly in all of the official fluidextracts of uva ursi which we made. It was usually of the same color and appearance and began to show in the bottom of the bottle within a few hours after the preparation was completed. Upon microscopic examination it was found to be largely crystalline. The fluidextract was found to be heavily loaded with suspended crystals similar to the sediment. They were needle-like to boat-shaped in appearance.

Microscopic observations were repeatedly made upon fresh lots of fluidextracts. After about twelve hours the reserve percolates consistently showed small microscopic masses but no crystals. Invariably, after twenty-four hours, however, small needle-like crystals, singly and in tufts, appeared. From this stage on they settled out continuously for long periods and constituted the bulk of the precipitate which formed in the fluidextract.

PROPERTIES OF THE CRYSTALLINE PRECIPITATE IN THE OFFICIAL FLIUDEXTRACT OF UVA URSI.

The crystalline character of the precipitate, which invariably forms in official fluidextracts of uva ursi has never been reported on, so far as we know. It may be described briefly as follows:

(*a*) Color, uniformly light tan to straw.

(*b*) Crystals, needle-like to boat-shaped, appearing singly and in tufts, or sheaves. (Plates I and II q. v.)

(*c*) Practically insoluble in all of the common solvents.

(*d*) Partly soluble in methyl alcohol containing about 20 per cent gaseous hydrochloric acid.

Plate I is a microphotograph of the crystals as commonly observed in the fluidextracts of uva ursi. Plate II is a picture of the crystalline precipitate after it had been treated with methyl alcohol containing 20 per cent gaseous hydrochloric acid and allowed to recrystallize.

INSOLUBLE GUM ISOLATED AND STUDIED.

The presence of a gum in uva ursi has been reported by numerous workers but none have said much about its properties. We were able to obtain it in the following manner.

The drug was percolated with ether. Upon the addition of alcohol to the ether percolate the gum precipitated and was easily coagulated with stirring. It may be described as follows: Light green in color, soluble in acetone and ether, insoluble in alcohol and water, decidedly adhesive and capable of being chewed like chewing gum.

URSON.

Urson was discovered in uva ursi and named by Trommsdorff in 1854 (1). Gintl (4) and Dodge (6) have also reported work upon urson.

We were able to obtain it by evaporating the ether-alcohol solution from which the gum just described, had been removed. Its properties are as follows: A white, amorphous, powder, melting point 240–241°, soluble in ether and alcohol, and insoluble in water.

It would seem that neither urson nor the insoluble gum are to be found, in any amounts, in the fluidextract of uva ursi, both being insoluble in the menstruum. Furthermore, both may be obtained from the exhausted marc. from which the fluidextract has been obtained.

THE EFFECT OF MENSTRUUMS UPON THE CHARACTER OF THE PRECIPITATE.

A series of nineteen fluidextracts was prepared. Nine of these were made with the official menstruums and all showed crystalline precipitates within a day. Nine of the remaining fluidextracts were made with menstruums composed of varying proportions of alcohol and glycerin. The precipitates in each case were non-crystalline. The last of the nineteen fluidextracts was prepared with an unofficial menstruum containing a large proportion of water. The precipitate which formed was crystalline.

From the results of these observations we may conclude, with Scoville, that fluidextracts made from tannin-bearing drugs should be highly alcoholic.

THE PRECIPITATE FROM A MANUFACTURER'S FLUIDEXTRACT.

A quantity of the precipitate of fluidextract of uva ursi was furnished by a manufacturer. It was a black, heavy, non-crystalline, partly liquid mass, and strongly acid to litmus. It gave tests for the presence of arbutin and tannin. Ashed samples gave positive tests for iron, aluminum, sodium and silica.

Quantitative studies indicated the following as being present:

Per cent of volatile substance	31.50
Per cent of ash	3.07
Per cent solubility in water	52.00
Per cent solubility in alcohol	43.10
Per cent solubility in dilute alcohol	58.00
Per cent tannin	4.83
Per cent arbutin	10.67

The tannin was determined according to the method of Löwenthal as given in "Tentative Methods of Analysis" (1930) of the A. O. A. C. (8). The arbutin was determined by the method of Zechner (7). Many of these two assays were made but are not reported here.

SUMMARY.

1. Fluidextract of Uva Ursi has been studied with respect to stability according to changes in p_H.

2. The crystalline character and solubility of the precipitate in official fluidextracts of Uva Ursi have been described.

3. An insoluble gum in Uva Ursi has been obtained and its physical properties studied.

4. Urson has been isolated and studied.

5. The effects of menstruums upon the character of the precipitate have been shown.

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THE WOOD OIL OF DOUGLAS FIR.*

BY CARL H. JOHNSON[1] AND RUSSELL A. CAIN.[2]

The volatile oil from the wood of *Pseudotsuga taxifolia* (Poir.) Britt., commonly known as Douglas fir has been examined by various investigators. The data obtained, however, in most cases is limited to the percentage yield of the oil and a few physical constants.

Frankforter (1) in 1906 extracted from 11.6 to 42.4 per cent of pitch from the wood in which was contained approximately 22 per cent of oil. From the data submitted it was apparent that the terpenes consisted entirely of alpha pinene.

In 1912 Benson (2) steam distilled the wood and obtained a colorless oil which he

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claimed was similar to French turpentine. He also obtained what he termed a "yellow oil," which contained approximately 48 per cent of terpineol.

In the following year Beath (3) collected an oleoresin by boring into the trunk of the tree, which on steam distillation yielded 15 per cent of volatile oil. A nitrosochloride was obtained which apparently indicated alpha pinene although the author failed to give its melting point.

The oil obtained by Schorger in 1917 (4) by distilling the oleoresin from the pockets in the wood contained alpha pinene, levo limonene and alpha terpineol. Benson and McCarthy (5) also investigated the oleoresin found in the pockets of the wood. The presence of levo alpha pinene and levo beta pinene was recorded based apparently upon the physical constants of the fractions since no derivatives were reported.

EXPERIMENTAL.

The oil used in this investigation was obtained by steam distilling selected pieces of pitchy wood collected during the autumn of 1935. From 40 pounds of fresh material there were obtained 675 cc. of oil which corresponded to a yield of 3.29 per cent.

The physical constants were determined in the usual manner d_{20} 0.8968; n_D^{20} 1.4773; $[\alpha]_D^{23}$ −41.50°; saponification number 2.3; acid number 1.6; ester number, calculated 0.7; per cent ester (calculated as terpinyl acetate) 0.1; saponification number after acetylization 99.0; per cent of total alcohol (calculated as terpineol) 28.9; per cent of free alcohol (calculated as terpineol) 28.7.

Free Acids.—Extraction of 50.0 cc. of oil with a 5 per cent aqueous solution of sodium carbonate yielded 1.955 Gm. of a brown viscous liquid which was strongly acid to litmus and possessed a decidedly pungent odor. Steam distillation of the residue resulted in the formation of an aqueous distillate on the surface of which floated a small amount of oily material. Several unsuccessful attempts were made to positively identify constituents in both of the layers of distillate, although the odor of the oily residue suggested the possible presence of at least traces of higher fatty acids such as caproic, caprylic, capric or lauric.

Phenols.—Extraction with a 5 per cent aqueous solution of sodium hydroxide yielded 0.1911 Gm. of dark brown residue which corresponded to 0.04 per cent of original oil. The residue did not respond to any of the general tests for phenols.

Fractionation.—The remaining oil which totaled 472 cc. was next subjected to fractional distillation at 25-mm. pressure. As a result of this fractionation the oil was divided into two parts, that which boiled below 100° C. and a higher boiling fraction which distilled above 100° C. The low boiling portion which amounted to 251 cc. and represented 50 per cent of the total oil was subjected to several refractionations.

Fraction No.	Boiling Point at 25 Mm.	Amount.	Sp. Gr. at 20° C.	$n_D^{20°}$.	$[\alpha]_D^{23}$.	Color.
I	60–72° C.	140 cc.	0.8590	1.4732	−52.70°	Colorless
II	72–75	35	0.8613	1.4762	−57.58	Colorless
III	75–82	28	0.8597	1.4793	−61.64	Colorless
IV	82–100	42	0.8624	1.4836	−53.33	Colorless

Levo Alpha Pinene.—A portion of the first fraction was oxidized by means of an 8 per cent aqueous solution of potassium permanganate according to the method of Tiemann and Semmler (6). The semicarbazone of pinonic acid was prepared in the usual manner by treating the residue resulting from the oxidation, with semicarbazide hydrochloride. The purified semicarbazone melted at 204° C., and thereby identified the fraction as consisting of alpha pinene.

Levo Camphene.—The first fraction, in addition to alpha pinene, contained a relatively large quantity of camphene. A portion of the fraction was hydrated according to the method of Bertram and Walbaum (7), which was modified to the extent that the non-hydrated oil was removed from the mixture. Saponification of the hydrated oil resulted in the formation of iso-

borneol, which when purified melted at 201° C. The phenylurethane derivative of the alcohol melted at 135° C. The identification, therefore, of isoborneol served to indicate the presence of camphene.

Levo Limonene.—Both the third and fourth fractions yielded a tetrabromide when brominated according to Wallach's method (8). The purified limonene tetrabromide melted at 101° C.

Saponification of the Higher Boiling Portion.—The higher boiling oil was saponified by heating with alcoholic potassium hydroxide. The saponified oil was washed, dried and subjected to fractional distillation, whereupon the following fractions were obtained:

Fraction No.	Boiling Point at 16 Mm.	Amount.	Sp. Gr. 20° C.	$n_D^{20°}$.	$[\alpha]_D^{20°}$.	Color.
I	100–125° C.	161 cc.	0.9417	1.4889	−42.83°	Yellowish
II	125–150	1	0.8620	1.5068	− 3.80	Yellow
III	150–200	8	0.8880	1.5204	−78.07	Amber
IV	200 and over	4	....	....	....	Tarry residue

Levo Alpha Terpineol.—The first fraction which distilled between 100° and 125° C., and represented approximately 92 per cent of the higher boiling portion of the wood oil was examined for terpineol according to the method of Wallach (9). The nitrosochloride which melted at 113° to 114° C. identified alpha terpineol as being the chief if not the sole constituent of the fraction.

Fraction II.—No attempts were made to identify the second fraction because of the small amount.

Fraction III.—The third fraction probably consisted of a sesquiterpene although no derivatives could be prepared.

Fraction IV.—This last portion possessed a burnt odor which indicated decomposition, hence no attempt was made to identify its components.

Combined Acids: Acetic Acid.—Acidification and steam distillation of the potassium hydroxide solution resulting from the saponification produced an aqueous distillate upon the surface of which there floated a small amount of insoluble material. Since no silver salt could be prepared from the insoluble distillate it was assumed that it did not consist of acids. The aqueous portion was made alkaline and evaporated to dryness. The residue obtained responded to the general qualitative tests for acetic acid.

SUMMARY.

The wood yielded 3.29 per cent of volatile oil which consisted of 50 per cent of terpenes and 32.2 per cent of an alcohol together with smaller amounts of probable sesquiterpenes. The oil contained about: 30 per cent levo alpha pinene; 6 per cent levo camphene; 14 per cent levo limonene; 32.2 per cent levo alpha terpineol, present almost entirely as the free alcohol; a small amount of higher boiling constituents probably sesquiterpenes. Acetic acid was present in the combined state.

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THE ASSAY OF SPIRIT OF PEPPERMINT.*

BY S. W. GOLDSTEIN AND W. F. REINDOLLAR.†

Although Spirit of Peppermint has been recognized in the last six Pharmacopœias, it was not until the U. S. P. XI became official that a mandatory assay for the volatile oil content was provided.

Briefly described, this assay determines the oil content on a 5-cc. portion in a Babcock bottle by adding one cc. of kerosene and sufficient calcium chloride solution to bring the oil layer within the graduations on the neck, centrifuging, reading the volume of the oil layer, and deducting five divisions (equivalent to 1 cc.) for the kerosene. The remaining number of divisions is multiplied by 4.2 to obtain the volume of oil of peppermint in 100 cc. of the spirit.

This assay is an application of the "precipitation" principle early applied by A. S. Mitchell (1) to flavoring extracts. Various modifications of this method by Howard (2), LaWall (3), Randall, *et al.* (4) and others, have appeared in the literature.

The basic principles involved are (A) a volatile oil is quantitatively precipitated from alcoholic solution when mixed with a large excess of concentrated calcium chloride solution, (B) it is completely soluble in kerosene, (C) the volume obtained by dissolving the oil in the volatile solvent is additive, *i. e.*, it is the sum of the volumes of the two constituents. LaWall did not obtain the relationship set forth in (C), observed a 5 per cent shrinkage, and suggested (5) that the factor 4.2, rather than 4 be employed. This value was incorporated in the U. S. P. assay.

The official assay has been applied to a number of spirits in this laboratory, both commercial and standard, with the observation that the results obtained were invariably high. This led to the conjecture that the factor 4.2 might be too great. The assay, however, is vague in certain other respects, which might lead to variations in results. The Pharmacopœia provides no formula for the acidified calcium chloride solution, employs kerosene when a purified kerosene reagent is described in the text, permits the use of uncalibrated Babcock bottles, and does not specify the manner in which the upper meniscus of the oil layer should be read. A systematic study was undertaken, therefore, for the purpose of evaluating the influence of these variables.

Five hundred cc. of a standard spirit was prepared from U. S. P. alcohol, garbled peppermint leaves and an oil of peppermint having the following properties:

Solubility: One volume of oil in 4 volumes 70% alcohol
Specific Gravity: 0.9149 at $\frac{25°}{25°}$ C.
Optical Rotation in a 100-mm. tube: −23.23° at 23° C.
Refractive Index: 1.4620 at 20° C.
Esters, calculated as menthyl acetate: 7.04%
Menthol: 54.3%.

The calcium chloride reagent was prepared by adding an excess of No. 4 mesh technical calcium chloride to water, containing 50 cc. concentrated hydrochloric acid in approximately one gallon. The liquid was employed without filtering out the excess of salt. Purified U. S. P. kerosene reagent was used to dissolve the oil.

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A series of twelve portions of standard spirit were assayed using the aforementioned reagents and employing the U. S. P. technique. The values were computed using both the values 4.2 and 4 as factors, and appear in Table I.

TABLE I.—RESULTS OBTAINED BY U. S. P. METHOD.

Bottle.	U. S. P. Factor 4.2.	Factor 4.	Bottle.	U. S. P. Factor 4.2.	Factor 4.
894	10.63	10.12	9	10.42	9.92
895	10.54	10.04	888	10.58	10.08
896	10.58	10.08	889	10.58	10.08
897	10.84	10.32	890	10.54	10.04
898	10.84	10.32	891	10.79	10.28
899	10.84	10.32	Average	10.64	10.13
2	10.46	9.96			

Inasmuch as the standard spirit contains 10 per cent by volume of oil the results obtained using the U. S. P. factor 4.2 are obviously too great, the values with the theoretical factor 4 being much closer to the correct result. However, as these latter results average 1.3 per cent too high, the presence of another source of error is indicated. This led to an investigation of the reagents employed.

Saturated calcium chloride solution, acidified with hydrochloric acid is the description given by the Pharmacopœia of the precipitating reagent. Aside from the facts that the quality of the salt and the concentration of acid are not specified, this solution is objectionable on other grounds. To assure saturation at all temperatures an excess of the salt must be present and the mixture should be shaken prior to use. This results in a turbid fluid which, if filtration is attempted, frequently crystallizes in the stem of the funnel. Hence, the substitution of a calcium chloride solution of lower concentration and having a definite formula was made. This reagent is about 75 per cent saturated, contains about 1 per cent free hydrochloric acid and is adjusted to a specific gravity of 1.36. Comparative results of the two solutions appear in Table II.

TABLE II.—RESULTS OBTAINED USING ACIDIFIED $CaCl_2$ SOLN., SP. GR. 1.36.

Bottle.	U. S. P. Factor 4.2.	Factor 4.	Bottle.	U. S. P. Factor 4.2.	Factor 4.
894	10.71	10.20	9	10.58	10.08
895	10.79	10.28	9	10.54	10.04
896	10.79	10.28	5	11.09	10.56
897	10.88	10.36	8	10.50	10.00
898	10.75	10.24	Average	10.74	10.23
899	10.96	10.44	Average—Table I	10.64	10.13
2	10.58	10.08			

As the average values obtained by using the two reagents lie close together and apparently fall within the limit of experimental error, either may be employed. The greater convenience in handling led to the use of the modified solution in the balance of these experiments.

An investigation of the possible variations caused by kerosene was next undertaken. The following experiment was made to learn the effect of temperature on kerosene expansion expressed in Babcock divisions.

A standard calibrated Babcock bottle was filled to the zero mark at 0° C., the temperature was allowed to rise, and readings were made at definite intervals. The values, plotting Babcock divisions as abscissæ against centigrade degrees as ordinates, appear on the accompanying graph.

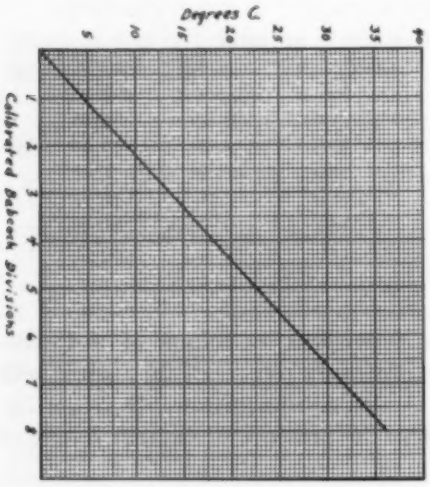

Fig. 1.

It was found that 50.8 cc. of kerosene expanded 7.9 divisions when the temperature was raised from 0° to 35.7° C. This is equivalent to an expansion of 0.0044 divisions per centigrade degree for one cc.—a completely negligible increment.

No reference is made as to how the reading of the upper meniscus should be made, and since this boundary has a definite thickness the following experiment was carried out.

Into each Babcock bottle was added one cc. of kerosene using a calibrated pipette, and sufficient calcium chloride reagent (specific gravity 1.36) to bring the oil within the graduated portion of the neck. The number of spaces occupied by the oil was determined by reading the lower curvature of the upper meniscus in one case and by recording the mean value of the upper and lower curvatures in the second.

TABLE III.—EFFECT OF READING LOWER PART AND MEAN MENISCUS.

Bottle.	Reading Obtained Using Mean Meniscus.	Reading Obtained Using Lower Meniscus.	Bottle.	Reading Obtained Using Mean Meniscus.	Reading Obtained Using Lower Meniscus.
888	5.05	5.00	893	5.13	5.07
889	5.07	5.01	3	5.16	5.09
890	5.06	5.01	5	5.15	5.10
891	5.15	5.10			
892	5.08	5.03	Average	5.12	5.05

The values obtained indicate that reading the lower curvature of the upper meniscus gives more accurate results.

In order to determine whether or not the alcohol present in spirit of peppermint affects the observed volume of kerosene, 4.5 cc. of alchohol, 1 cc. of purified kerosene and acidified calcium chloride solution (specific gravity 1.36) were mixed and treated in the prescribed manner. Here, as in all subsequent work, the lower curvature of the upper meniscus was read.

TABLE IV.—RESULTS OBTAINED WITH KEROSENE AND ALCOHOL.

Bottle.	Volume in Babcock Units.	Bottle.	Volume in Babcock Units.
888	5.00	893	5.09
889	4.98	3	5.16
890	4.97	5	5.10
891	5.01		
892	5.07	Average	5.05

The added alcohol does not appear to be responsible for any change in the observed volume of the kerosene layer.

In order to determine what effect peppermint oil would have on the observed volume a similar experiment was made omitting alcohol and including 0.5 cc. of oil. The results are recorded as observed readings and are also calculated to cc. of oil in 100 cc. spirit.

TABLE V.—RESULTS OBTAINED WITH KEROSENE AND PEPPERMINT OIL.

Bottle.	Babcock Units.	Cc. Oil/100 Cc. "Spirit." Factor 4.2.	Factor 4.
888	7.46	10.33	9.84
889	7.50	10.50	10.00
890	7.51	10.54	10.04
891	7.61	10.96	10.44
3	7.65	11.13	10.60
5	7.56	10.75	10.24
Average	7.55	10.70	10.19

The results here, as well as in preceding tables, indicate that if there is any deviation from the additive effect with regard to volume it is in the direction of expansion rather than contraction.

The study of kerosene behavior was concluded with an investigation intended to show whether different kerosenes gave different readings and whether the results with the purified and unpurified products were similar. Five commercial kerosenes were purchased from different sources, a portion of each was purified, and tests were made using both purified and non-purified oil.

TABLE VI.—RESULTS OBTAINED WITH DIFFERENT KEROSENES.

Kerosene (Commercial) No.	Factor 4.2.	Factor 4.	Kerosene (Purified No.)	Factor 4.2.	Factor 4.
1	10.64	10.14	1	10.69	10.18
2	10.74	10.23	2	10.61	10.11
3	10.66	10.15	3	10.64	10.14
4	10.70	10.19	4	10.70	10.19
5	10.64	10.14	5	10.67	10.16
Average	10.68	10.17		10.66	10.13

The use of different kerosenes, whether purified or not, does not apparently influence the results. However, since all the commercial kerosenes did not meet the U. S. P. requirement for color (specific gravity and distillation value were satisfactory), and since the Pharmacopœia describes a purified reagent it is felt that the purified product should be employed in the assay.

The one remaining important factor which is not recognized in the official assay is the variation in the graduation of Babcock bottles. In order to determine this effect, standard bottles (calibrated at the United States Bureau of Standards and at the Bureau of Chemistry of the Maryland State Health Department) were used throughout the investigation. These factors which varied from +0.55 per cent to −2.00 per cent, were not used in the earlier work but were later applied to the accumulated data, the comparative results appearing on page 630.

It will be noted that using the factor 4 and applying the calibration corrections yield results closely approximating theoretical figures. As a further illustration of this fact the data obtained on a number of commercial spirits employing the modi-

TABLE VII.—EFFECT OF CALIBRATION OF BABCOCK BOTTLES.

Average Values Using Factors 4.2 and 4 before and after Applying Calibration Correction Factors.

	Before.		After.	
	4.2.	4.	4.2.	4.
Table I	10.64	10.13	10.53	10.03
Table II	10.74	10.23	10.65	10.15
Table VI	10.70	10.19	10.38	9.87
Table VII				
(comm.)	10.68	10.17	10.49	9.99
(purified)	10.66	10.13	10.44	9.96

Average Values in Babcock Units before and after Applying Calibration Correction Factors.

	Before.		After.	
Table III	5.12	5.05	5.06	5.00
Table IV	5.05		5.00	

fied calcium chloride solution, purified kerosene, and reading the lower curvature of the upper meniscus are presented. Although the true values of these spirits must remain unknown, it may be generally assumed that the high values obtained using the U. S. P. factor and neglecting the calibration correction are fictitious.

TABLE VIII.

Bottle No.	Calibration Factor, %.	U. S. P. XI without Correction for Calibration.	U. S. P. XI with Correction for Calibration.	Factor 4 without Correction.	Factor 4 with Correction.
888	−0.31	10.92	10.84	10.42	10.32
889	−0.56	11.26	11.09	10.72	10.56
890	−0.44	11.21	11.09	10.68	10.56
891	−1.25	11.93	11.51	11.36	10.96
892	−0.31	11.72	11.63	11.16	11.08
893	−1.13	11.76	11.38	11.20	10.84
894	−0.31	10.54	10.46	10.04	9.96
895	−0.06	11.00	11.00	10.48	10.48
896	−0.19	10.96	10.92	10.44	10.40
897	−0.75	11.13	10.88	10.60	10.36
898	−0.56	11.00	10.84	10.48	10.32
899	−1.25	11.34	10.92	10.80	10.40
3	−2.00	11.42	10.79	10.88	10.28
29	−0.52	11.09	10.92	10.56	10.40
9	+0.34	11.13	11.26	10.60	10.72
5	−1.74	12.64	12.05	12.04	11.48

As a result of these investigations it is believed that the official assay may be improved and rendered more accurate by adopting the following modifications:

(1) The substitution of the value 4 for the present factor 4.2;
(2) The use of calibrated glassware;
(3) The adoption of the modified calcium chloride solution and purified kerosene in place of the present reagents;
(4) Specifying that the oil column reading be made from the lower meniscus to the lower curvature of the upper meniscus.

CONCLUSIONS.

1. The official assay for Spirit of Peppermint yields results that are too high.
2. A modified assay has been devised employing specific reagents and cali-

brated glassware, by which results in close agreement with the theoretical values may be obtained.

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THE PHARMACOLOGY OF PYRETHRUM FLOWERS.*[1]

BY HARRY ROSEN AND MARVIN R. THOMPSON.[2]

The literature pertaining to the chemistry and pharmacology of pyrethrum flowers is reviewed in the original thesis and by other recent writers (1) (2), and hence will not be repeated here. This report is intended to embrace only the experimental studies described in the thesis.

In the course of the experimental work it was noted that pyrethrum powder or solutions exposed to air deteriorated rapidly. It was also observed that roaches and flies apparently protected from contact with the powder but not from possible vapors, readily exhibited symptoms of pyrethrum action. The possibility of an active volatile fraction was therefore investigated.

EXPERIMENTAL.

Six hundred grams of insect flowers were steam distilled and 4 liters of distillate collected in 250-cc. fractions. Some of the early fractions on injection into the ventral lymph sac of frogs showed toxicity. These combined distillates were saturated with sodium chloride, extracted with petroleum ether, and the solvent allowed to evaporate at room temperature. The residue was taken up in 25 cc. alcohol and precipitated by the addition of saturated sodium chloride solution, a light brown semi-solid mass resulting. This also showed some toxicity to frogs but was not investigated further because of a very meager yield. Four more samples of insect flowers were likewise steam distilled, but the distillates showed no toxicity to frogs and were found to exert no action on isolated rabbit intestine. The frog and intestine test methods are described in detail elsewhere in this paper.

The remainder of each of these steam distillates was saturated with sodium chloride and divided into two portions. One portion was extracted with petroleum ether and assayed chemically and the other was extracted with purified kerosene and assayed by the Peet-Grady fly

TABLE I.—RESULTS OF STEAM DISTILLATE ASSAYS.

Sample	Assay of Drug before Distillation. Fly Method.		Chemical Method.			Fly Method.		Assay of Steam Distillate. Chemical Method.		
			Total Pyrethrins.	Pyrethrin I.	Pyrethrin II.			Total Pyrethrins.	Pyrethrin I.	Pyrethrin II.
A	68%	Kill	0.81%	0.361%	0.449%	3%	Kill	0.0015%	0.001%	0.0005%
D	83%	Kill	0.80%	0.344%	0.456%	4%	Kill	0.0035%	0.0025%	0.0010%
F	88%	Kill	0.83%	0.365%	0.465%	5%	Kill	0.0036%	0.002%	0.0016%
J	84%	Kill	0.835%	0.365%	0.470%	6%	Kill	0.0031%	0.0017%	0.0014%

* Scientific Section, A. PH. A., Dallas meeting, 1936.

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[2] Abstracted from a thesis submitted in May 1936 by Harry Rosen to the Faculty of the Graduate School of the University of Maryland in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

method. The following table shows the steam distillates to be inactive, since the actual results appearing in the table for the distillates are negative in the range of significant figures.

Control determinations by the fly method, using only purified kerosene, resulted in a fly mortality of 4–7%.

Distillation of various alcoholic percolates and macerates was also resorted to, but the results failed to prove the existence of an active volatile fraction in the drug.

THE SITE OF ACTION OF PYRETHRUM FLOWERS.

Pyrethrum flowers were found to be toxic to both warm- and cold-blooded animals, depending upon the dosage and the route of administration employed.

A hydro-alcoholic suspension of an extract of pyrethrum flowers, when injected into the ventral lymph sac of a frog produced, in a few minutes a very marked increase in reflex excitability resembling that resulting from the administration of strychnine. The increased reflex excitability soon began to pass into a state of decreased reflex excitability and in a short time the animal was completely paralyzed, with death rapidly ensuing.

If the spinal cord of the frog was destroyed before administration of the drug, the first symptoms of increased reflex excitability were not manifested. However, if the brain was destroyed, leaving the spinal cord intact, these symptoms were observed as in the normal frog. This evidence indicated that the drug exerted its action on the spinal cord.

An olive oil suspension of an active extract injected subcutaneously into white rats produced effects analagous to those observed in the frog. A typical protocol follows:

3:55—Olive oil suspension representing 12 mg. pyrethrum flowers per Gm. rat administered subcutaneously
4:00—Symptoms of distress
4:05—Increased reflex excitability
4:15—Animal in definite clonic convulsive state
4:40—Clonic convulsions ceased and paralysis developed
4:45—Respiration ceased
4:47—Cardiac arrest.

Cats after having been fed insect flowers mixed with food to the extent of 10%, over long periods of time, showed no toxic symptoms and appeared normal in all respects. However, relatively large doses of solutions of pyrethrum extracts administered to cats, intravenously or intraperitoneally, quickly produced death, especially by the intravenous route.

The following is a typical protocol showing symptoms produced by intraperitoneal injection to cats:

10:43—Olive oil suspension of active pyrethrum extract representing 4 Gm. of the flowers per Kg. cat administered intraperitoneally
10:48—Visible signs of discomfort
12:00—Abnormal movement of hind legs in locomotion and hyperactive response to mechanical stimuli in these limbs
1:00—Hind legs becoming hypoactive and forelegs hyperactive
2:30—Both fore and hind legs non-responsive to mechanical stimuli, fast and labored respiration, no readily demonstrable signs of cerebral depression, corneal reflex apparently still normal
3:00—Signs of cerebral depression—corneal reflex depressed
4:12—Respiratory failure
4:15—Cessation of heart beat.

The symptoms produced in the foregoing experiments indicated that insect flowers produce an ascending paralysis of the spinal cord, preceded by a transitory stimulation.

Experimentation with a view of determining action on the autonomic nervous system was conducted, but significant effects were not apparent from reasonable doses. Large intravenous doses of pyrethrum flowers produced no change in blood pressure of the cat. Due to this fact it appears that the drug has no action on the autonomic nervous system supplying circulation, since any significant effect at all would have shown an alteration in blood pressure. Three such experiments were performed.

PROOF OF SITE OF ACTION OF PYRETHRUM FLOWERS.

The first experiments to prove the site of action of insect flowers were concerned with its effects on the gastrocnemius muscle and sciatic nerve of the frog.

APPARATUS.

The apparatus consisted of a Harvard inductorium, platinum electrodes to stimulate the muscle, non-polarizable boot-electrodes for stimulation of the nerve, a moist chamber and a dry cell of 1.23 volts and 0.08 amperes as a source of current.

PROCEDURE.

One leg of a spinal frog, excepting the sciatic nerve, was ligated as high up as possible and amputated just below the ligature. A muscle nerve preparation was made and the minimal stimulus which elicited response of the muscle was determined by stimulation of the nerve with the boot electrodes. Likewise, by use of the platinum electrodes, the minimal stimulus causing response in the muscle was determined by direct stimulation. The results were recorded as the number of centimeters the secondary was removed from the primary coil, and also the number of degrees the secondary was rotated from the iso-axial plane of the primary coil.

A sample of pyrethrum, in a hydro-alcoholic macerate containing 10% alcohol, of which 0.0002 Gm. per Gm. of frog was pre-determined to produce paralysis in 25 to 35 minutes, was injected in the same dosage into the ventral lymph sac of the frog. After 45 minutes the remaining leg was amputated and the tests for minimal stimuli were conducted as for the first leg.

Another group of frogs was used as controls. The same recordings were made as for the experimental frogs.

TABLE II.—RESULTS OF DRUG ACTION ON NERVE AND MUSCLE.

No.	Gm. Wt.	Sex.	Before Drug. Leg.	Nerve.	Muscle.	After Drug. Leg.	Nerve.	Muscle.
1	19	M.	Left	10 cm. 45°	8.0 cm. 40°	Right	10 cm. 55°	10.0 cm. 0°
2	16	F.	Left	11 cm. 40°	7.8 cm. 0°	Right	11 cm. 40°	7.6 cm. 0°
3	13	F.	Left	9 cm. 20°	7.0 cm. 0°	Right	9 cm. 30°	7.0 cm. 0°
4	19	M.	Right	10 cm. 0°	8.0 cm. 25°	Left	9 cm. 20°	8.0 cm. 25°
5	15	M.	Right	11 cm. 35°	7.2 cm. 0°	Left	11 cm. 35°	7.1 cm. 0°
6	18	M.	Right	10 cm. 20°	7.6 cm. 0°	Left	12 cm. 55°	7.8 cm. 0°
				Controls with 10% Alcohol.				
7	18	F.	Left	12 cm. 60°	7.5 cm. 0°	Right	12 cm. 30°	7.0 cm. 0°
8	17	M.	Left	12 cm. 40°	8.0 cm. 10°	Right	12 cm. 40°	10.0 cm. 10°
9	20	M.	Right	13 cm. 35°	8.2 cm. 20°	Left	12 cm. 35°	7.9 cm. 0°
10	17	M.	Right	11 cm. 55°	7.5 cm. 0°	Left	11 cm. 55°	8.4 cm. 0°
11	17	F.	Right	10 cm. 55°	7.7 cm. 0°	Left	12 cm. 30°	8.4 cm. 0°

On examination of Table II, it is seen that small differences in intensity of stimulus necessary to elicit response in the nerve and muscle before and after the drug are sometimes present. However, comparable differences are also found in the controls, and thus it is readily seen that the drug exerts no action of any consequence on the muscle or the motor nerve.

For further studies, spinal frogs were again used, but here, the spinal cord and sciatic nerve were observed for effects produced by the drug.

APPARATUS.

The same inductorium and source of current were employed as above, but fine copper wire electrodes were used to stimulate the spinal cord and platinum electrodes were used to stimulate the sciatic nerve.

PROCEDURE.

The spinal cord, above the junction of the sciatic nerve (5th lumbar vertebra), and the sciatic nerve of one leg were exposed. The threshold stimulus was determined for each and the drug administered as in the previous experiments. Then at various intervals, recordings of the threshold stimuli were made. Here, also, control frogs injected with 10% alcohol were tested and the results compared to those obtained from the frogs exposed to the drug.

TABLE III.—RESULTS OF DRUG ACTION ON CORD AND NERVE.

No.	Gm. Wt.	Sex.	Before Drug. Cord.	Nerve.	Time.	After Drug. Cord.	Nerve.
1	21	M.	8.4 cm. 15°	10.3 cm. 50°	31 Min.	6.2 cm. 0°	10.3 cm. 55°
2	15	M.	8.4 cm. 10°	11 cm. 55°	28 "	7.1 cm. 0°	11.0 cm. 40°
3	21	F.	9.0 cm. 0°	9 cm. 30°	20 "	7.0 cm. 0°	9.0 cm. 35°
					45 "	2.0 cm. 0°	9.0 cm. 30°
4	23	F.	9.0 cm. 0°	9 cm. 40°	28 "	6.3 cm. 0°	9.0 cm. 30°
					54 "	5.5 cm. 0°	9.0 cm. 50°
5	24	M.	9.0 cm. 20°	9 cm. 15°	40 "	6.8 cm. 0°	9.0 cm. 40°
6	25	M.	5.8 cm. 0°	8.5 cm. 25°	30 "	4.6 cm. 0°	8.5 cm. 30°
					62 "	2.2 cm. 0°	8.5 cm. 35°
7	23	M.	4.1 cm. 0°	9 cm. 10°	46 "	2.3 cm. 0°	9.0 cm. 60°
8	22	F.	8.5 cm. 15°	9 cm. 45°	41 "	6.3 cm. 0°	9.0 cm. 55°
9	19	F.	7.0 cm. 0°	8.4 cm. 30°	60 "	5.3 cm. 0°	8.4 cm. 40°
10	22	F.	9.4 cm. 0°	10 cm. 35°	45 "	8.2 cm. 0°	10.0 cm. 40°
					65 "	6.4 cm. 0°	10.0 cm. 40°
			Controls with 10% Alcohol.				
1	20	M.	7.3 cm. 60°	10.8 cm. 25°	30 Min.	7.2 cm. 0°	10.9 cm. 30°
2	26	M.	7.0 cm. 0°	8.2 cm. 0°	30 "	7.0 cm. 0°	8.2 cm. 0°
					90 "	7.2 cm. 0°	8.3 cm. 45°
3	27	F.	7.3 cm. 0°	9.0 cm. 20°	37 "	7.2 cm. 0°	9 cm. 35°
					87 "	6.8 cm. 0°	9 cm. 45°
4	25	F.	8.5 cm. 15°	10.0 cm. 50°	38 "	8.5 cm. 50°	10 cm. 55°
					56 "	8.5 cm. 50°	10 cm. 40°
5	22	M.	9 cm. 30°	10.0 cm. 20°	40 "	9 cm. 0°	10 cm. 25°
					75 "	9 cm. 15°	10 cm. 40°
6	22	F.	7.8 cm. 0°	10.0 cm. 20°	34 "	7.7 cm. 0°	10 cm. 40°
					69 "	7.7 cm. 0°	10 cm. 45°

Table III shows again that the motor nerve is not affected, but the spinal cord is definitely depressed, because the secondary coil had to be brought closer to the primary coil of the inductorium (greater stimulus) in order to carry the impulse down the cord and over the sciatic nerve to elicit a response of the muscle. This depression is an ascending one, since it was observed in intact animals that the hind limbs and then the fore limbs were paralyzed. The paralysis, therefore, involves the anterior horn of the cord, since direct stimulation of the cord showed the paralysis.

Proof of the presence or absence of action on the posterior portion of the cord was next undertaken.

APPARATUS.

The same inductorium as above was used with two dry cells of 3.0 volts and 51 amperes, platinum electrodes being used for purposes of stimulation.

PROCEDURE.

Two frogs were used for each experiment one being a spinal frog and the other a completely pithed frog, both sciatic nerves of the spinal frog and the right sciatic nerve of the completely pithed frog being exposed. The left sciatic nerve of the spinal frog and the right sciatic nerve of the completely pithed frog were contacted by means of a wire bridge and the stimulus was applied to the right sciatic nerve of the spinal frog. The threshold stimulus necessary to pass over the posterior portion of the cord of the spinal frog, down the left sciatic nerve, into the right sciatic nerve of the completely pithed frog, and producing a response in the leg, was ascertained. Then the drug solution was injected into the ventral lymph sac of the spinal frog and at various intervals the threshold was again determined.

Control frogs were also used here and the results compared to those obtained from the frogs injected with pyrethrum flowers. The results were recorded the same as those in Tables II and III.

TABLE IV.—RESULTS OF DRUG ACTION ON POSTERIOR HORN OF SPINAL CORD.

No.	Gm. Wt.	Sex.	Before Drug.	Time.	After Drug.
1	25	M.	5.0 cm. 0°	128 Min.	2.5 cm. 0°
2	29	F.	7.4 cm. 0°	82 "	4.7 cm. 0°
3	25	F.	4.9 cm. 0°	80 "	3.7 cm. 0°
4	25	F.	3.8 cm. 0°	115 "	*0.2 cm. 0°
5	24	M.	5.7 cm. 0°	69 "	4.1 cm. 0°
6	24	M.	4.2 cm. 0°	90 "	*0.2 cm. 0°
7	25	M.	5.3 cm. 0°	130 "	2.0 cm. 0°
8	19	M.	7.0 cm. 0°	59 "	5.6 cm. 0°
9	24	M.	6.7 cm. 0°	96 "	2.8 cm. 0°
10	25	F.	6.3 cm. 0°	127 "	4.8 cm. 0°
			Control Frogs.		
1	20	M.	6.5 cm. 0°	130 Min.	6.2 cm. 0°
2	25	F.	5.5 cm. 0°	114 "	5.8 cm. 0°
3	24	F.	6.3 cm. 0°	72 "	6.2 cm. 0°
4	25	M.	7.1 cm. 0°	104 "	6.8 cm. 0°
5	26	M.	8.3 cm. 0°	140 "	7.9 cm. 0°

* No response here. Secondary coil could not be moved closer to primary coil.

Analysis of Table IV shows that depression of the posterior portion of the spinal cord caused by drug action is far in excess of the slight changes occurring in the control frogs over a period of time, proving that the sensory portion of the spinal cord is depressed by the drug.

A review of all results thus far obtained shows that pyrethrum flowers exert no changes on the threshold for either striated muscle or motor nerves. However, the drug does depress both the anterior and posterior portions of the cord after a transitory period of stimulation.

This does not entirely dismiss the possibility of changes in the phases of an isotonic contraction of striated muscle. The threshold stimulus may not be changed, but nevertheless the phases through which a muscle passes in an isotonic contraction may be altered.

In determining the effects of the drug on phases of contraction of striated muscle, both cold- and warm-blooded animals were used.

PROCEDURE.

For the cold-blooded animal experiments, a muscle nerve preparation of a frog's gastrocnemius muscle was made and stimulated directly with platinum electrodes, recording the phases by means of a kymograph. The muscle was irrigated with pyrethrum in frog Ringer's solution and again the phases of contraction were recorded and compared to the original phases before drug action.

In the experiments with warm-blooded animals, anesthetized cats were used. The proximal portion of the gastrocnemius muscle was left intact, but the distal tendons were detached and connected to a muscle lever. The phases of contraction produced by direct stimulation with platinum electrodes were recorded and the muscle was then irrigated with pyrethrum solution. After considerable irrigation the phases were again recorded, the results being compared to the original.

Analyses of the phases of contraction of the frog and cat muscles show no significant changes after exposure of the muscles to the action of pyrethrum flowers.

After the effects of the drug on striated muscle were ascertained, the action of pyrethrum flowers on intestinal muscle was next determined.

PROCEDURE.

Segments of rabbit intestine from the pyloric portion each about one centimeter long, were bathed in 50 cc. of Tyrode's solution maintained at 37.5° C. After a suitable control recording had been obtained, pyrethrum solution was added and the results noted.

It was found that pyrethrum produced a decrease in amplitude of contraction and a decrease in tonus of isolated rabbit intestine.

For further localization of this action, the response of the muscle to a definite dose of 1% barium chloride solution was observed, the barium solution was replaced by new Tyrode's solution and pyrethrum added. After an elapse of ten minutes the original dose of barium chloride was added and, at two-minute intervals, two larger doses of barium chloride were administered.

This procedure showed that the action of barium which is directly on the muscle is inhibited by pyrethrum, thus indicating that pyrethrum acts directly on intestinal musculature.

THE BIOLOGICAL ASSAY OF PYRETHRUM FLOWERS.

The assay of pyrethrum flowers has been the object of much research in recent years, numerous chemical and biological methods having been proposed and used by various test laboratories. The best chemical methods and the fly method which appears to be the peer of the biological assay procedures, require either elaborate apparatus or consume very much time. In addition, many investigators are unable to agree on the superior suitability of any one method.

In view of these facts, Chevalier (3), and Chevalier and Ripert (4) have suggested the use of the frog as a test object, and Perrot and Gaudin (5) and Rigal (6) have used isolated rabbit intestine as a means of evaluating pyrethrum flowers.

In this work, both of these suggestions were further investigated and a method has been developed from each.

THE OVER NIGHT FROG METHOD OF ASSAY.

Various symptoms produced by pyrethrum flowers on the frog were considered as possible end-points in determining the potency of unknown samples of drug and it was finally concluded that over night mortality was the best end-point. This necessitated the preparation of a mortality curve in order to compare the relative strengths of an unknown pyrethrum and the one that would be used as a standard.

PREPARATION OF MORTALITY CURVE—APPARATUS.

The apparatus consisted of a storage tank for the frogs with constant running water at a temperature below 15° C. in order to reduce the metabolic rate of the frogs, so that feeding would

not be necessary. A large tank, the temperature of which could be maintained at 20° C. ± 0 .5° C., equipped with individual compartments, was used for keeping the frogs over night after administration of the drug. The individual compartments had no bottom and were placed on wire screens, immersed in the water to a depth of about one centimeter.

ANIMALS.

The frogs used in the preparation of the mortality curve weighed from 15 to 35 Gm. and were stored in the tank, with running water below 15° C., for one week before use.

PROCEDURE.

Seven series of frogs, each series of one sex weighing within a range of 5 Gm., were divided into eight groups, each group of equal number ranging from 10 to 25 frogs depending on the number available. On different days, 24 hours before use, each series of frogs was removed from the storage tank and placed in the individual compartments at 20° C. ± 0.5° C. Before administration of the drug, each frog was dried with a towel, the urine expressed and the weight recorded within one-half gram. The drug was used as a 10% macerate in alcohol, diluted with distilled water so that the solution contained less than 25% alcohol and so that no frog received more than 0.02 cc. per Gm. The same 10% alcoholic macerate was used in all the seven series of frogs but the dilutions were prepared as needed for each group of frogs. Eight doses, one for each group of each series, were selected so that the lowest dose produced no mortality and the highest dose produced 100% mortality. The frogs of each group were injected in the ventral lymph sac with the assigned doses and each frog was placed in its separate compartment. The following day, the frogs were examined and the percentage mortality was recorded for each dose. A curve was plotted for each series of frogs, and all of the curves were then superimposed on a 50% point. Finally, the various percentage mortalities were averaged and a composite curve of all the individual results was prepared.

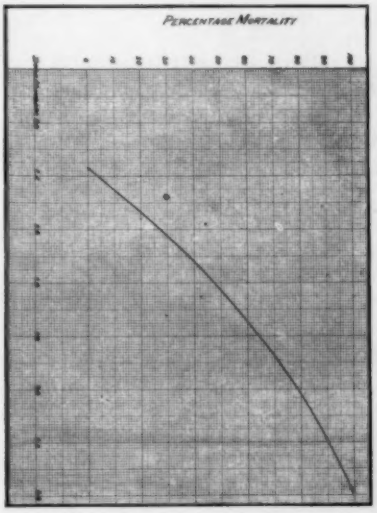

Fig. 1.—Composite of all frog mortality curves.

Table V.—Dose Numbers Corresponding to Percentage Mortality.

Per Cent Mortality.	Dose Number.	Per Cent Mortality.	Dose Number.
0	2.17	52	2.65
4	2.20	56	2.70
8	2.23	60	2.75
12	2.27	64	2.80
16	2.30	68	2.85
20	2.33	72	2.91
24	2.37	76	2.97
28	2.41	80	3.03
32	2.44	84	3.10
36	2.48	88	3.17
40	2.52	92	3.24
44	2.56	96	3.32
48	2.60	100	3.40

From the composite curve, dose numbers for all possible percentage mortalities, based on the use of 25 frogs, were calculated and recorded for use in obtaining the potency of an unknown pyrethrum in terms of a standard pyrethrum.

ASSAY PROCEDURE—APPARATUS AND ANIMALS.

The apparatus and animal requirements are the same as for the preparation of the curves.

SOLUTIONS.

The drug, if not already ground, is reduced to a No. 40, or finer, powder. Five grams of both the standard and unknown powders are accurately weighed and placed in separate 25-cc. volumetric flasks. Sufficient alcohol is added to each to make 25 cc. and the solutions are placed in the dark at 1–2° C. for 24 hours, with occasional agitation, after which they are ready for use. The solution is brought to room temperature before use and the supernatant fluid is decanted without shaking.

ASSAY PROCEDURE.

Frogs weighing between 15 and 35 Gm. and of one sex are used in the assay. For any one determination, the frogs must all weigh within a range of five Gm. The diluted solutions for injection must not have an alcohol content of more than 25% and if necessary, any excess alcohol is removed with a current of air. Not less than 0.01 cc. nor more than 0.02 cc. per Gm. frog may be injected, no frog receiving a dose of less than 0.25 cc. The dose of both standard and unknown producing a mortality of approximately 50% is determined by injecting varying doses into groups of three frogs to each dose. The frogs are kept below 15° C. until 24 hours before the assay and then removed to a 20° C. ± 0.5° C. temperature. They are dried with a towel, urine expressed and weighed to within 0.5 Gm. just prior to their use. After orientation of the 50% mortality dose for both standard and unknown, 50 frogs of the above specifications are selected, and 25 injected with each, the standard and unknown. The following day, the mortality percentages are determined and by means of the curve-dose numbers the potency of the unknown is determined in terms of the standard. The percentage mortalities may be from 20% to 80% but never below or above these figures. The frogs which recover may be used again in preliminary orientation of dosage, but never in final determinations.

DISCUSSION OF A TYPICAL FROG ASSAY.

From experience, it has been found that pyrethrum flowers do not have as wide a range of potency in terms of a good commercial sample, which may be chosen for a standard, as do many other drugs. The potency may vary from 0% to 150% but it has been most unusual to obtain a specimen that assayed above this figure. For this reason, in orienting the over night M. L. D., not so wide a range of doses is necessary and one preliminary determination of three frogs to each dose often suffices, especially if the assayist has carried out recent determinations and knows the approximate M. L. D. of the standard. If such is not the case, two preliminary tests may be necessary. The object is to find the dose which will result in a mortality as near 50% as possible.

For the sake of explanation of the preliminary assay, let it be assumed from previous results, that 0.0004 Gm. per Gm. frog, of the standard, resulted in approximately 50% mortality. This dose can be used for the standard in the final assay, since this figure does not vary greatly in monthly periods. For the unknown, doses are selected which are based on 0.0004 Gm. per Gm. frog as the 50% M. L. D. of a 100% drug or the equivalent of the standard. The doses of the unknown are calculated on the basis of possibilities of 25, 50, 75, 100, 125 and 150 per cent of the standard. The solution is properly diluted and injected into the ventral lymph sacs of three frogs for each dose. The following day the results were found to be, for example, as follows:

Suspected Potency.	Grams per Gram Frog.	Results of 3 Frogs.
150%	0.000266	− − −
125%	0.000320	− + −
100%	0.000400	+ − +
75%	0.000533	+ + −
50%	0.000800	+ + +
25%	0.001600	+ + +

These results show that the 50% M. L. D. of the unknown lies between 0.000320 and 0.00040 Gm. drug per Gm. frog.

For the final assay, the average, 0.00036 Gm. per Gm. frog, is used as the dose and 25 frogs are injected. Likewise, 25 frogs are injected with 0.00040 Gm. standard per Gm. frog.

The following day it is found, for example, that the standard produced 52% mortality and the unknown produced 36% mortality.

Consulting Table V, it is seen that
0.004 Gm. (S) = 52% mortality = 2.65 dose number
0.00036 Gm. (X) = 36% mortality = 2.48 dose number

Thus 0.00036 Gm. (X) multiplied by $\frac{2.65}{2.48}$ = 0.004 Gm. (S)

0.000384 Gm. (X) = 0.004 Gm. (S)
1.0 Gm. (X) = 1.042 Gm. (S)
(X) = 104% of (S)

THE BARIUM INHIBITION OR ISOLATED RABBIT INTESTINE METHOD OF ASSAY.

It has been previously shown that pyrethrum flowers decrease amplitude and tonus of rabbit intestine, and that this action is exerted directly on the muscle, Fig. 1, since the effect of barium on the intestine is inhibited by pyrethrum. On further investigation, it was found that this inhibition occurs quantitatively and for this reason, the reaction has been utilized as the basis of a method of biological assay.

APPARATUS.

The apparatus for this assay consisted of an isolated tissue bath equipped with two 50-cc. tissue chambers and a constant temperature control. The tissue chambers were so equipped that they could be emptied and refilled with the tissue bathing fluid without undue exposure of the tissue to air. The chambers were also equipped with an oxygen supply which could be regulated as necessary for various tissues.

TISSUE.

The tissue was obtained from the pyloric portion of the rabbit's intestine, the rabbit being preferably a mature one.

SOLUTIONS.

The pyrethrum solutions for this assay were prepared as for the frog method. The barium solution consisted of a suitable strength (usually 1%) solution of barium chloride in distilled water and Tyrode's solution was used as the bathing fluid for the tissues.

ASSAY PROCEDURE.

The rabbit is killed by a blow on the head and approximately 50 cm. of the pyloric portion of the intestine are removed. The extirpated tissue is placed in a beaker containing Tyrode's solution and may be used immediately. The remainder of the tissue, after the first strips are taken for use, is kept at 1–2° C. Two 1.5–2-cm. portions of the intestine, both of equal length, are cut and suspended in each of the tissue chambers and the upper ends are attached to suitable

magnifying levers in order to record the results. The oxygen is adjusted as necessary for the two strips of tissue, care being taken that both receive exactly the same supply. The temperature is maintained between 37.5° C. and 38° C. Tension is applied, the same to both tissues, as necessary and the tissue is allowed to relax. Then similar doses of barium are added to each chamber, usually 0.2 to 0.4 cc. being sufficient, and a significant response of 2 to 4 minutes' duration is recorded. A 1% solution of barium chloride usually suffices, but occasionally it is necessary to use a 2% or 3% solution. After recording the first response the bathing fluid is removed, new fluid is introduced and the tissues are allowed to relax. Finally equal doses, smaller than the first, are added to each chamber and the responses are recorded. These latter doses enable the assayist to determine whether or not the tissues are reacting consistently, and also insure against a maximal response, which is shown by the second response being less than the first. If the reactions are consistent and a submaximal response has been obtained, these responses are accepted as controls.

The tissues are again freed of the Tyrode's solution containing the barium, and new Tyrode's solution is introduced. Next, the unknown pyrethrum solution is added to one chamber immediately after washing; and one minute later the standard pyrethrum solution is added to the other chamber. Usually, 0.25 cc. to 0.5 cc. of a 1 to 3 dilution of the stock solution of pyrethrum (Tyrode's solution being the diluent) is satisfactory to inhibit the quantities of barium suggested above. Ten minutes later, the original submaximal dose of barium is added to each chamber containing, respectively, the above-mentioned pyrethrum solutions. After the tissues return to the control line, two subsequent doses of barium are added to each chamber. The second and the third doses are usually twice and three times the strength of the first dose, respectively. From the degree of inhibition produced by both the standard and unknown pyrethrum solutions, the potency of the unknown is determined in terms of the standard. New strips are required for each determination, since the tissues do not recover within a reasonable period of time.

A TYPICAL ASSAY BY THE BARIUM INHIBITION METHOD.

Although the intestine removed from the rabbit for use in this procedure is always satisfactory for one day's use, it was possible, with patience, to successfully use strips from the same intestine for two or even three days. However, on the second or third day, the tissue responds very slowly and for the saving of time it is recommended that new tissue be used each day.

New strips are used for each determination, although evidence is at hand which shows that the drug effects can be washed out and the tissues used again. The washing and subsequent recovery are very prolonged, and since an abundance of tissue is available for one day's work, the loss of time in waiting for recovery is not justifiable.

For the purpose of conveying some idea as to the procedure for obtaining the potency of an unknown pyrethrum powder by this method, figures of an actual assay are presented.

A dilution of I, representing 0.6666 Gm. pyrethrum flowers per cc., was assayed in terms of a dilution of A, representing 0.7123 Gm. pyrethrum flowers per cc.

In the first determination, 0.3 cc. of each was used and it was found that I produced greater inhibition of response of the intestine to barium, than did A, thus being more than 107% of the potency of A.

Then, the dose of A was increased to 0.4 cc. while the original dose of I was retained, and as a result this dose of A was more potent than 0.3 cc. of I, showing I to be less than 142% of A.

In the next determination, a dose of 0.25 cc. of I was compared to 0.3 cc. of A and was found to be more potent than the dose of A, being therefore more than 128% of A.

From these results it is seen that the potency of I is between 128% and 142% of A. For commercial purposes, any further attempts to orient the potency are not

necessary and an average of the two figures, which is 135%, may be assigned to I. Further increase in the number of determinations permit of somewhat greater precision.

The dilutions of the stock macerate of the drug must be prepared each day as they lose potency rapidly after dilution.

The percentage inhibition produced by the pyrethrum in this assay is of great importance. If too much inhibition of barium is obtained, the relative potencies of the two preparations cannot be easily deduced. The pyrethrum dosage must be so selected as to provide a definite barium response at the end of the ten-minute period.

The use of more than one dose of barium following the ten-minute elapse of time for the production of pyrethrum paralysis, is advisable in all assays. This helps clarify results and removes much of the possibility of misinterpretation of potency.

This method of assay is accurate, without difficulty, within plus or minus 10%. On various occasions the writers obtained an accuracy within plus or minus 5%, when assaying different dilutions of one preparation prepared by other members of the laboratory, the writers being totally without knowledge of their relative potencies.

APPLICATION OF THE NEW BIOASSAY METHODS.

Ten commercial samples of pyrethrum flowers were obtained and identified as A to J, inclusive. Sample A, which was considered to be a good commercial sample, was used as the standard. It was preserved in ampuls, in the dark, at 1–2° C. Each ampul contained approximately 5 Gm. which is the quantity indicated for use in the assay procedures.

The remaining nine samples were assayed in terms of A by the two new methods and in addition, by the Seil chemical method (7) and the Peet-Grady fly method (8).

TABLE VI.—RESULTS OF ASSAYS.

Sample.	Total Pyrethrin Content.	Pyrethrin I Content.	Pyrethrin II Content.	Fly Kill in 24 Hours.	Potency in Terms of Total Pyrethrins.	Potency in Terms of Pyrethrin I Content.	Potency in Terms of Pyrethrin II Content.	Potency by Frog Method.	Potency by Intestine Method.
A	0.81 %	0.361%	0.449%	68%	...	...	...	..	...
B	0.32 %	0.133%	0.187%	48%	40%	37%	42%	41%	25%
C	0.121%	0.062%	0.059%	16%	15%	17%	14%	25%	25%
D	0.80 %	0.344%	0.456%	83%	99%	95%	102%	86%	99%
E	0.87 %	0.371%	0.499%	89%	107%	103%	111%	62%	133%
F	0.83 %	0.365%	0.465%	88%	102%	101%	104%	98%	91%
G	0.87 %	0.375%	0.495%	80%	107%	104%	110%	89%	109%
H	0.76 %	0.350%	0.410%	69%	94%	97%	91%	86%	107%
I	0.77 %	0.364%	0.406%	77%	95%	101%	94%	64%	135%
J	0.835%	0.365%	0.470%	84%	103%	101%	105%	60%	125%

DISCUSSION OF RESULTS OF ASSAYS.

Table VI shows that the results obtained by the frog and isolated rabbit intestine methods of assay are not always in good agreement with those resulting from the chemical assay.

The frog assays, while showing good agreement with the chemical assay, involving six of the samples, show low results in the remaining three samples.

The isolated intestine determinations show good agreement with the chemical assays in six of the comparisons and show no great disagreement in the remaining three tests.

It is significant to note that the disagreements of both of the biological methods with the chemical method occur in the same samples, the frog assay showing a lower potency and the isolated intestine assay showing a higher potency than the chemical assay.

In some instances, the percentage fly kill shows some agreement with the assay results of the other methods, but the absence of a standard of comparison deprives the fly results of any great significance, showing only the relative positive or negative fly killing powers of a sample of pyrethrum flowers.

SUMMARY AND CONCLUSIONS.

1. Pyrethrum, by the methods so far employed, was found to contain no volatile active constituent.

2. Pyrethrum flowers are toxic to both warm- and cold-blooded animals, depending upon the dosage and route of administration.

3. Cold-blooded animals (frogs and insects) are much more susceptible to the action of pyrethrum than warm-blooded animals (rats and cats).

4. Skeletal muscle and the motor nerves supplying this type of muscle are not affected by pyrethrum flowers.

5. Following toxic doses, pyrethrum flowers produce a transitory stimulation of both the anterior and posterior horns of the spinal cord, followed by an intense depression.

6. The principal site of action of pyrethrum is the spinal cord. The character of the action may be described as a transitory stimulation followed by depression and paralysis of a distinctly ascending type, ultimately reaching the medullary centers.

7. The autonomic nervous system appears not to be directly affected by pyrethrum flowers. Any alterations in function of autonomically controlled organs are slight, and are induced reflexly.

8. Rabbit intestine is depressed by pyrethrum flowers, the drug exerting its action directly on the musculature.

9. Two new methods of assay, the Over Night Frog and Isolated Rabbit Intestine methods have been developed and used for assay purposes.

10. Nine samples of pyrethrum flowers have been assayed in terms of a reference standard, by the Seil chemical method, Peet-Grady fly method and the two new biological assay methods.

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The authors wish to acknowledge indebtedness to Dr. E. G. Vanden Bosche for coöperation in the preparation of the frog mortality curves, and to Mr. A. E. Badertscher, of McCormick and Co. Inc., who kindly supplied the pyrethrum flowers and carried out the fly and chemical methods of assay.

A PRELIMINARY STUDY OF TINCTURE OF CANTHARIDES.*

BY LESLIE M. OHMART.[1]

INTRODUCTION.

To accord with the newly adopted international standards for tinctures of potent drugs, the U. S. Pharmacopœia VIII directed that 10 Gm. of cantharides be used in preparing 100 cc. of the tincture. This was twice the amount of drug used in the tincture previously official. Alcohol was directed to be used as the menstruum. Although no special investigation was made at the time of adoption, the practicability of a 10% tincture was soon questioned. The relative insolubility of cantharidin in alcohol (approximately 1–1333) indicated incomplete extraction. For many years, the official tincture and possible substitutes, therefore, have been under investigation.

Scoville (1) reported that the tincture of cantharides made by the official method represented but from $^1/_2$ to $^2/_3$ of the cantharidin content of the drug used and recommended the use of glacial acetic acid in the menstruum as an aid to extraction.

Eberhardt (2) found the official method inadequate and obtained relatively poor results with an acid-alcohol menstruum. He reported complete exhaustion of the drug by treating with caustic alkali and extracting with dilute alcohol but the resulting tincture was weak in vesicating power. A tincture which was actively vesicant and which fully represented the cantharidin content of the drug was obtained by treating the drug with glacial acetic acid and acetone and extracting with acetone.

Scoville (3) gave the results of further study of tincture of cantharides. Fifteen experimental tinctures were made, using mixtures of several solvents as menstrua. None of these experiments was successful in producing a tincture which fully represented the drug. Digestion, preliminary to percolation, was found to increase the yield of cantharidin. The use of glacial acetic acid in the menstruum was again recommended.

Scoville (4) reported eighteen experiments. One of these, made by digestion and maceration, and employing in succession, water acidulated with glacial acetic acid, chloroform and alcohol, produced complete exhaustion but the investigator was unable to duplicate his success when using other samples of cantharides. A mixture of glacial acetic acid and alcohol, 1 in 10, was again recommended as the most satisfactory menstruum.

Scoville (5) obtained approximately 90% exhaustion by extracting cantharides with glacial acetic acid and acetic ether in a Soxhlet apparatus, adjusting the volume with alcohol.

In 1919, Nitardy (6) used a menstruum of potassium hydroxide, water and alcohol suggested by Squibb (7) for the preparation of a fluidextract of cantharides. The tincture obtained was satisfactorily vesicant and contained 99 mg. cantharidin in 100 cc. The cantharidin content of the drug from which the tincture was made was not stated.

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* Section on Practical Pharmacy and Dispensing, A. PH. A., Dallas meeting, 1936.

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In 1921, Nitardy (8) reported that wide variation in the results obtained from the use of a hydro-alcoholic menstruum containing potassium hydroxide prompted him to withdraw his recommendation of 1919.

As the result of a series of experiments in which he used chloroform, acetone and glacial acetic acid as aids to extraction, Nitardy (9) recommended the use of glacial acetic acid in the menstruum for the official tincture of cantharides.

In the U. S. Pharmacopœia X, the menstruum for tincture of cantharides was directed to be composed of 1 volume of glacial acetic acid and 19 volumes of alcohol. In the U. S. Pharmacopœia XI, this was increased to 1 volume of glacial acetic acid and 9 volumes of alcohol. Tincture of cantharides prepared by the present official method has a strong acetous odor; chiefly because of the odor, numerous objections to the present formula have been voiced.

Feeling that the work previously done on this subject, while valuable, was not conclusive, the writer undertook further investigation in the hope of devising a practical method which would yield a tincture of cantharides free from the objectionable features of the present official tincture.

EXPERIMENTAL.

Two lots of cantharides were procured and assayed by the U. S. P. method. Drug A, a fine powder, yielded 0.662% cantharidin. Drug B, a very fine powder, yielded 1.165% cantharidin.

Nine tinctures were prepared from Drug A and assayed according to Scoville's (3) modification of the method of Self and Greenish (10). The methods of preparation, menstrua used and assay results are shown in the following table:

TABLE I.

	Method.	Menstruum.	Cantharidin Content, Maximum—0.0622 Gm.	Percentage of Extraction.
1.	Percolation	Alcohol	0.0160 Gm.	25.7%
2.	Percolation	Alcohol + 2.0% CH_3COOH	0.0362 Gm.	58.2%
3.	Percolation	Alcohol + 4.0% CH_3COOH	0.0420 Gm.	67.5%
4.	Percolation	Alcohol + 7.0% CH_3COOH	0.0400 Gm.	64.2%
5.	Percolation	Alcohol + 10.0% CH_3COOH	0.0508 Gm.	81.7%
6.	Percolation	Alcohol + 0.5% HCl	0.0333 Gm.	53.5%
7.	Percolation	Alcohol + 1.0% HCl	0.0439 Gm.	70.7%
8.	Percolation	Alcohol + 1.5% HCl	0.0469 Gm.	75.4%
9.	Maceration	Alcohol + 1.0% HCl	0.0589 Gm.	94.7%

In an attempt to verify the favorable results obtained by the use of hydrochloric acid in the menstruum, four tinctures were prepared from Drug B and assayed in the same manner. The methods of preparation, menstrua used and assay results are shown in Table II.

TABLE II.

	Method.	Menstruum.	Cantharidin Content. Maximum—0.1165 Gm.	Percentage of Extraction.
1.	Percolation	Alcohol + 0.5% HCl	0.1056 Gm.	90.6%
2.	Percolation	Alcohol + 1.0% HCl	0.1043 Gm.	89.5%
3.	Percolation	Alcohol + 1.5% HCl	0.1026 Gm.	88.1%
4.	Maceration	Alcohol + 1.0% HCl	0.1126 Gm.	96.7%

In preparing the tinctures from Drug B, it was found necessary to mix three parts of purified sand with one part of the drug to facilitate the passage of the menstruum. No sand was used in the preparation of the tinctures from Drug A but it probably could have been used to advantage. The relatively low cantharidin content of tinctures 6, 7 and 8 may be due, in part, to the tendency of powdered cantharides to form masses through which the menstruum penetrates with difficulty. The assay result obtained in tincture 9 tends to confirm this view.

The method by which the tinctures were assayed, while it is perhaps the best yet devised, is long and tedious and considerable practice is necessary to develop the skill required for consistent results. It is recommended that an attempt be made to devise a method of volumetric assay.

SUMMARY.

1. Earlier investigators found that a 10% tincture of cantharides, extracted with alcohol, did not fully represent the drug from which made.

2. The present Pharmacopœia directs a menstruum of alcohol containing 10% of glacial acetic acid. This is objectionable in that the tincture so made has a strong acetous odor.

3. Experiments were conducted in an attempt to devise an alternate method.

4. Certain of these experiments tended to confirm the conclusions of earlier investigators regarding a menstruum of alcohol or of alcohol and glacial acetic acid.

5. Certain of the experiments indicate that a menstruum of alcohol containing 1/2% to 1% of hydrochloric acid will yield a satisfactory tincture.

6. Maceration gave a higher percentage of extraction than did percolation.

CONCLUSIONS.

1. The use of 10% of glacial acetic acid in the menstruum for the official tincture of cantharides seems to be unwarranted.

2. A menstruum of alcohol containing 1/2% to 1% of hydrochloric acid appears to yield a satisfactory tincture of cantharides.

3. Further study should be made to determine the minimum amount of hydrochloric acid necessary for complete extraction.

4. Maceration is superior to the official process of percolation as a method of extraction for cantharides.

ABSTRACT OF DISCUSSION.

William J. Husa remarked that the use of hydrochloric acid is important.

C. O. Lee inquired whether the author had found a satisfactory assay for the tincture. The author replied that this paper represented preliminary work.

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THE ANTISEPTIC VALUE OF CALOMEL OINTMENT N. F. V AND N. F. VI.*

BY LEWIS C. BRITT.[1]

The need of adequate measures for the control of venereal diseases has been given much publicity in recent months. The publicity has been accompanied in some instances by a quieter but very important investigation of the efficacy of remedies offered for sale for the prevention of diseases in recently exposed individuals.

Among prophylactic preparations submitted for examination in Oregon were several samples of calomel ointment. Some of these were prepared by the N. F. VI formula, which uses a base of petrolatum and hydrous wool fat, and some were prepared by the N. F. V formula, which uses only petrolatum as a base. Examination of the two ointments by the Agar Cup-Plate Method of the U. S. D. A.,[2] using *Staphylococcus aureus* as a test organism and incubating for 24 hours at 37° C., showed that the ointments prepared by the N. F. VI formula were not nearly so effective as the ones prepared by the N. F. V method. The wide-spread use of this preparation as a prophylactic for venereal diseases and its intended omission from the list of prophylactics approved for sale in Oregon by the State Board of Pharmacy indicated an immediate need for study of the N. F. VI preparation.

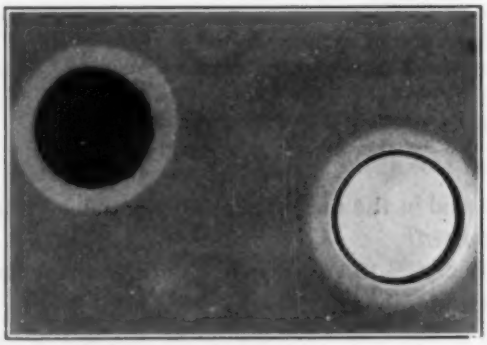

Fig. 1.—Calomel ointment, N. F. V.

Results of typical tests of the antiseptic action of the N. F. V and VI calomel ointments are shown in Figs. 1 and 2.

The clear zone surrounding the dark-centered figure in each case represents the inhibitory action of the ointments. The clear-centered figure represents a phenol control to which all prophylactics sold in Oregon must conform. The phenol control was adopted, in preference to a minimum inhibitory zone expressed in millimeters, as it automatically makes needed adjustments for variation in the virulency of the organism, variation in constitution of the media, temperature variations and other minor factors which will influence the width of the inhibitory zone.

The impaired activity of the N. F. VI ointment may be traced directly to the addition of the hydrous wool fat. However, the manner in which the hydrous wool fat acts is not so apparent. The natural affinity of wool fat for water or an increase in the viscosity of the preparation both appear as possible explanations for the decreased activity. To determine which of these possibilities was the actual one, calomel ointments were prepared with 30 per cent anhydrous wool fat and petrola-

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* Section on Practical Pharmacy and Dispensing, A. PH. A.

[1] Chemist, Oregon State Board of Pharmacy.

[2] United States Department of Agriculture, Circular No. 198 (1931).

tum, and with petrolatum containing 5 and 10 per cent white wax. If the affinity of the wool fat for water is responsible for the impaired activity there should be a marked decline in the antiseptic action of the preparation containing it and little or no change in the ointments prepared with white wax. If an increase in viscosity is responsible, all three preparations should show a decreased activity. The results of these tests are shown in Figs. 3, 4 and 5.

It is indicated from these tests that the variation in activity of the N. F. V and N. F. VI calomel ointments is due to an increase in viscosity caused by the addition of hydrous wool fat in the latter preparation.

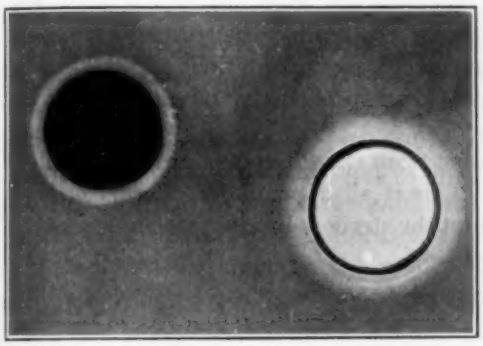

Fig. 2.—Calomel ointment, N. F. VI.

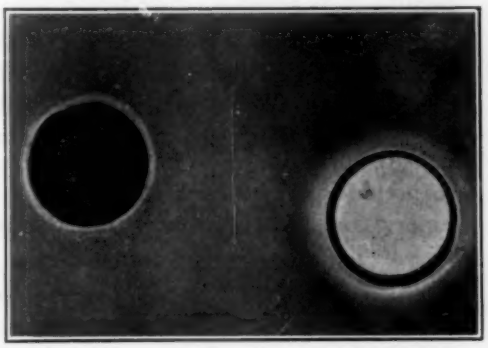

Fig. 3.—Calomel ointment, 30 per cent anhydrous wool fat.

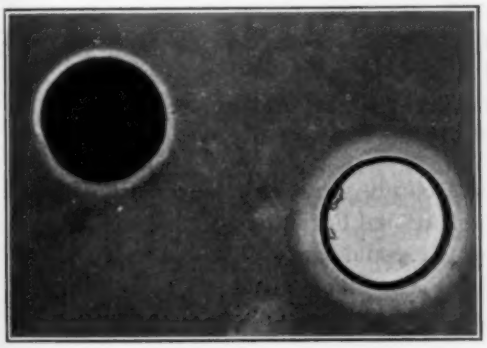

Fig. 4.—Calomel ointment, 5 per cent white wax and petrolatum.

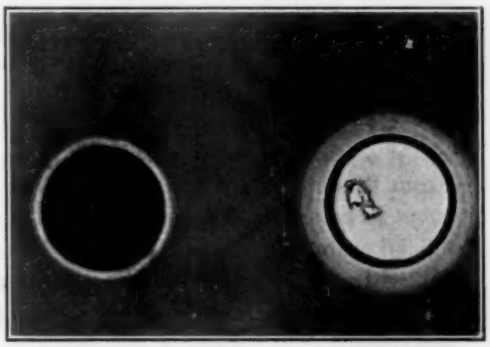

Fig. 5.—Calomel ointment, 10 per cent white wax and petrolatum.

SUMMARY.

1. N. F. VI calomel ointment is not so effective an antiseptic as the N. F. V preparation.

2. N. F. VI calomel ointment does not show sufficient antiseptic action to be classed as a prophylactic for venereal diseases in the state of Oregon.

3. Immediate need for revision of the present formula for calomel ointment is indicated.

STERILE PARENTERAL FLUIDS AND THE HOSPITAL PHARMACIST.*

BY EVLYN GRAY SCOTT.[1]

During the past few years there has been a steady increase in the amount of parenteral fluids used in hospitals and from it has grown the problem of securing a safe, economical and easily prepared supply. When only small amounts were required the sterile solutions were generally prepared by graduate and student nurses in the operating division, mainly because this department prepared sterile supplies for the hospital rather than any desire or special knowledge on their part to do so. As the demand grew larger the preparation of the required amounts became more difficult. The percentage of reactions was large but little was known as to their cause. Some of the more progressive hospitals tried to solve this by putting the responsibility for the preparation of sterile solutions on the pharmaceutical department. Others walked around the problem by buying them from commercial concerns.

At our hospital we have a separate room from the Pharmacy proper in which to prepare, sterilize and store solutions. This is all done under pharmaceutical supervision. At the present time the bulk of the sterile solutions prepared consists of:

Sodium Chloride 0.85% and 5%
Dextrose 6%
Dextrose 3% and Sodium Chloride 0.425%
Hartmann's
Soluble Iodophthalein
Sucrose 50%
Sodium Citrate 2½%
Sodium Iodide 12½%
Procaine Hydrochloride ½%, 1%, 2% and 4%
Saturated Boric Acid
Distilled Water
Glycerin.

From this one can readily see that we have barely scratched the surface of what is yet to be accomplished in this field. The National Formulary VI has many more official ampuls which, if the demand warranted, could easily be added to the above list with a material saving to the hospital. The chief objections to commercial solutions are their prohibitive price and their lack of flexibility for every type of emergency.

For the first half of November 1935 our hospital used approximately one million cc. of the above-named solutions prepared at a production cost of 0.008 cents per cc. This price included every item of expense except that of the original equipment, such as still, sterilizer, cupboards and sinks. If this original equipment cost is spread over several years and then added to the cost of solutions the price is still well under that of commercial solutions and has the added advantage of being easily and quickly adopted to the needs of the individual hospital.

The solutions are prepared from fresh, singly distilled water. This water must

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* Section, Practical Pharmacy and Dispensing, A. PH. A., Dallas meeting, 1936.

[1] St. Lukes Hospital (Pharmacy), Cleveland, Ohio.

meet the U. S. P. requirements for distilled water. The important test in this case is that for organic or pyrogenic material. It is a known fact that a great number of the reported reactions have been caused by water containing pyrogen which is a product of living bacteria. Although the writer believes that some safe, easy way can be found to store distilled water, at the present time she finds it easier to mix, filter and sterilize the solution within two hours from the time that the water is distilled. Although sterilization prevents the formation of pyrogen it cannot remove that which has already accumulated.

The chemicals used are of C.P., Reagent or U. S. P. quality. The proper amounts are weighed, the solution is well mixed and then filtered directly into pyrex flasks. A fine grade of filter paper such as Carl Schleicher and Schüll No. 575 or ground glass Jena filters is used. The flasks are prepared, if new, by treating them with sulfuric dichromate solution, otherwise the flasks are washed on bottle washers similar to those found in soda fountains and then inverted on racks to drain dry. If these flasks are not used within several hours they are washed again. After the proper amount of solution is placed in the flask it is then capped with two pieces of vegetable parchment and one of cellophane. The flasks are never filled more than two-thirds of the volume, because of the danger of wetting the tops by bubbling as the pressure is being lowered in the sterilizer. The paper is held in place by string which is tied as tightly as possible at the top of the flask and again about an inch down the neck. These flasks are labeled by fastening printed paper labels around the neck of the flask. The various procaine hydrochloride solutions are put up in hard glass bottles with aluminum screw caps or rubber vaccine stoppers. The intravenous solutions are outdated two weeks from the day in which they are sterilized. Although the solution remains sterile as long as the top remains intact there is a slow loss of water by evaporation and a change of p_H value due to the air, so that it is believed safer not to hold the solutions too long before using. There are several methods of permanently sealing these flasks that are being used by various hospitals at the present time (1). All solutions are sterilized between 115° and 121° C. Amounts up to 500 cc. are sterilized 10 minutes, those between 500 and 1000 cc. for 15 minutes, and between 1000 and 2000 cc. for 20 minutes. Liquids such as oils are sterilized by dry heat for one hour at 150° C. Solutions that deteriorate when heated are made sterile by putting through a Seitz filter that has been properly prepared.

All intravenous solutions are administered by fitting the flasks containing the proper solutions with a special two-hole stopper (2), fitted with the necessary glass connectors, rubber tubing and glass adaptor with needle. The needle is inserted by a doctor and the solution flows in by means of gravity.

This form of medication, regardless of the purity of the solution itself, might become contaminated unless the rubber tubing and glass connectors have been properly treated and prepared. To rid the rubber tubing of its sulfur bloom it is necessary to treat it with some alkali and then to wash well and treat with an acid. I think the plan established by the University Hospital of Syracuse University—to place all this under one supervision (3)—has suggested the logical method of attack. Our pharmaceutical responsibility should not end with the solution but should be made to include these various sterile sets which are necessary in using these carefully prepared solutions.

REFERENCES.

(1) Walter, Carl W., M.D., *J. A. M. A.*, 106, 1982 (1936).
(2) Walter, Carl W., M.D., *Ibid.*, 104, 1688 (1935).
(3) Mordell, J. Solon, JOUR. A. PH. A., 50, 24 (1935).

WHAT DIFFERENCE DOES A CENTURY MAKE?*

BY JOHN E. KRAMER.[1]

Yesteryear's events, especially those of interest to a group such as the Historical Section of the AMERICAN PHARMACEUTICAL ASSOCIATION, are of more interest and value when compared to current events. For instance, historians point out that pharmacy in the early nineteenth century was probably at a lower ebb than it had been for many years, with ready sale for cheap drugs, and substitution, adulteration and other evils prevalent. Contemporaries contend rather contemptuously that pharmacy is again at a rather low ebb to-day.

A recent event in the newspaper world affords us an opportunity to study the situation. On March 25, 1936, the *Philadelphia Inquirer*, one of the larger daily news sheets of the City of Brotherly Love, celebrated the hundredth birthday of the *Philadelphia Public Ledger*, which the *Inquirer* had merged with, or, to state it correctly, had absorbed on April 15, 1934.

With its regular issue of March 25, 1936, the *Inquirer* included a facsimile of the small, four-page, closely printed, unillustrated inaugural issue of the *Ledger* of 1836. The following are three of the advertisements that can be read only with eyesight good enough to overcome and decipher the atrocious print.

> PAINTS, DYE STUFFS, &c.—100 brls. English Venitian Red; 40 kegs do. Chrome Green, dry; 2000 lbs. Verdigris; 300 lbs. Verdigris, distilled; 20 cases China Vermillion; 100 brls. Yellow Ochre; 10 casks French Stone Ochre; 25 do. Pumice Stone; 25 do. Rotten do; 10 do. Turkey Umber; 20 tons Camwood, in stick; 10 do. Red. Sanders, in do; 25 do. Fustic, in stick; with an assortment of oil ground dye woods, paints, anuriatic and nitric acid, aquafortis, oil Vitriol, &c., for sale by G. D. Wetherill & Co., 56 North Front st.
>
> CROMMELIN & JENKINS, No. 154 North Third st., offer for sale, of their own manufacture, English and American, Mustard, in jars, kegs and bottles, Chocolate, No. 1 and 2, in boxes and halves; Ground Ginger, brls. and kegs; Cayenne and Black Pepper; ground Alspice; Cinnamon and Cloves; prepared Cocoa; Flour, Rice and Nutmegs; all of which they can sell lower than any other manufactory in this city.
>
> N.B. Orders from any part of the United States will be thankfully received and punctually attended to.
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>
> SCARLET FEVER—SMALL POX—A cure for these diseases has been discovered by an eminent French Physician, from whence it has been introduced into this country, and thus far has never failed. The article may be procured at No. 121 North Second st.
>
> ATTENTION—No sooner than a good medicine is offered and the public begin to receive the benefit, and before the proprietor has time to receive a re-

* Section on Historical Pharmacy, A. PH. A., Dallas meeting, 1936.

[1] Registrar, Philadelphia College of Pharmacy and Science.

muneration for his expenses, straightway competition and imitation accompanied with deception is set in motion to the injury both to the proprietor and the medicine, and an imposition on the public. Such has been the case in this city and perhaps in some others, with an article which has been before the public for three or four years past as a cure for Dyspepsia, prepared by C. Joy, and known as JOY'S ANTI-DYSPEPTIC ELIXIR. Persons who have received the desired benefit and wish to recommend it to their friends will please caution them that the genuine article is put up in bottles, impressed on the sides "JOY'S ELIXIR," "ANTI-DYSPEPTIC," and sold at the General Agency, No. 84 North Third Street, wholesale and retail.

Also, the French vegetable remedy known as THE PELGEIAN REMEDY, although it has not been offered in this city more than about one year, yet a half dozen or more imitators are at work already selling an inferior article; but the genuine "Remedy" is sold at the same agency as Joy's Elixir, and requires the same care in obtaining the article pure.

The unparalleled and astonishing success accompanying the use of the Pelgeian remedy in every case where it has been properly administered, has no doubt been the cause of so many imitators, and it will be highly interesting to patients to procure the article compounded from the best materials. The following diseases have already been cured by this remedy:—Quinsey, Scarlet Fever, Dysentery, Cholera Morbus, Cholic, Cancer, Worms, Fits, Small Pox, Fever and Ague, Influenza, Measles, Inflamed Eyes, Sock Head Ache, long continued and extreme pains in the face and jaw.

JOHN R. SLEEPER, *Proprietor*,
No. 121 North Second street.

Ad number one indicates the presence of the well-known combination drug and paint industry. Ad number two indicates the presence of price competition. Ad number three indicates the presence, a century ago, of counter prescribing, quackery, fraud and misrepresentation.

The passage of a hundred years marked many changes for the betterment of the profession, yet a look at just three of the many advertisements for March 25, 1936, makes us pause and wonder at the perfect panaceas, pleasing prices and personal prescribing still to be had for the asking in some drug stores.

NOW I EAT
FRIED PORK
Upset Stomach Goes
In Jiffy With.....

These tablets are wonder-workers on the bowels, causing a normal action, carrying off the waste and poisonous matter in one's system.

If you have a pale face, sallow look, dull eyes, pimples, coated tongue, headaches, a listless, no-good feeling, all out of sorts, inactive bowels, take one or two of.....tablets, etc., etc.

ACID IN YOUR BLOOD
KILLS HEALTH AND PEP
KIDNEYS OFTEN TO BLAME

Because of its world-wide and unusual success, ... is offered under a written guarantee to do the work to your complete satisfaction in 8 days or money back on return of empty package. Under the written guarantee you can put..... to the test and see exactly what it can do in your particular case. You must feel younger, stronger and better than you have in a long time—you must feel that .....has done this work thoroughly and completely, or you merely return the

empty package and it costs you nothing. You are the sole judge of your own satisfaction. With.....there is no long waiting for results because it is scientifically prepared to act directly on the Kidneys as a diuretic. For that reason most people report a remarkable improvement within the first 48 hours, and complete satisfaction within 8 days. .....costs only 3¢ a dose at druggists and as the guarantee protects you completely, you should not take chances with cheap, inferior or irritating drugs or delay. Telephone your druggist for guaranteed.....(Pronounced .....) to-day.

Three other items of general interest found in the reprint of the century-old paper are copied here.

Brandy and water, and cigars—a fast trotting horse, a pocket book with bank notes, gaining and late hours—are the rocks on which are shipwrecked many bright hopes and alluring prospects—the fond anticipations of parents, and the realization of anxiously desired blessings.—MAJOR NOAH.

A well-known toper fell into a fever, which greatly increased his thirst; when the physicians were deliberating on the means of removing both, the patient gravely begged that they would confine themselves to the office and task of removing the fever, leaving to himself the care of the thirst.

The Congressional news up to this date possesses not the slightest interest—Congress seems determined to fritter away its time, instead of rendering it profitable to the nation—shame on such tardy legislation.

Now ask yourself, as I did, what difference does a century make?

THE FINDINGS OF A DRUG CLERK ACTING IN THE GUISE OF THE INQUIRING REPORTER.*

BY GEORGE A. STALL.

It is most interesting to learn the opinions of the public in the various walks of life, regardless of color, creed, race, age or profession, of the present-day drug store as compared with the apothecary shop of yesteryears.

Looking through the memorandum of answers to questions asked, mention will be made only of a few of the more interesting ones.

Question: What is your opinion of the drug store of to-day as compared with the drug store of the days gone by?

Answer: Why, the drug store to-day is no drug store at all; it is a general merchandise store, more like a department store.

Question: Do you have the same confidence in the present-day general drug store as you had in the drug store of yesterday, when the drug store was purely a drug store?

Answer: No; in the first place, in the olden days one could go to the apothecary shop and talk with the doctor (druggist) and rely on what he advised; he was a distinguished gentleman and knew what he was talking about. To-day, one hardly feels that way, because for the most part, the customer is met by a young fellow, full of pep, raring to go, full of ideas, who knows it all. He is inexperienced and not capable, his mind is too full of merchandising to concentrate on pharmacy. He does not have the dignity of the pharmacist of the past; one does not feel one can trust him.

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* Section on Commercial Interests, A. PH. A., Dallas meeting, 1936.

One man gave me this story: He walked into one of the stores, which is looked upon to-day as a drug store, and asked for 100 two-grain quinine pills. The clerk, one of the commercialistic variety, waited on him. He went behind the counter, looked through several drawers in the open-to-view of the customer prescription counter, came back and told the customer he was sorry they did not have the two-grain quinine pills, but that the only thing they had was two-grain sulfate of quinine pills.—Do not censure the clerk, but yourself! In hiring your clerks, try to get experienced ones, and even if it costs you a few dollars more per week it will be worth it.

While traveling through the Southwest, recently, a visit was made to a chain store for the purpose of purchasing a package of cigarettes and learning what was to be learned. A lady patron wished to purchase 100 of a certain brand of Aspirin Tablets. The clerk produced them, but instead of wrapping them wrapped 100 other aspirin tablets. When he handed the package to the customer, she politely asked: "Why did you not give me the tablets I asked for?" "Well," replied the clerk, "I gave you our brand; they are just as good, and you surely don't want to pay the difference in price for the special brand." The lady told him she wanted the brand asked for, and if there was any reason why he could not sell them to her she would go elsewhere. Following the controversy, the manager of the shop walked over and reprimanded the clerk for not having hidden from view the package of the special brand while he wrapped the package. Splendid work on the part of the manager, but what can one expect? Having finished his purchase, the inquiring reporter left the shop.

The next one approached happened to be a society editor of a local paper. Between assignments he had joined the usual crowd of professional loafers engaged in watching the progress of a building construction. Rather an interesting fellow. While his work was usually among women folks, talking at luncheons, teas, doings of bridge clubs, etc., he at least had a good idea regarding drug stores. His answer to the question asked is summarized: "The shoemaker should stick to the last. Herr Von Hitler is right in the respect that the stove man should sell stoves, the grocery man sell groceries, etc. He went quite deeply into the subject about 1¢ sales, etc."

Now it would not have been fair not to interview a few drug store proprietors. Here is what one pharmacist told me. To begin, let me say—his store, while not a chain, was one which had all the appearances of one. The question I asked was: "What is the greatest problem you are confronted with to-day?" His answer was: "I don't know, I have trouble with all of them." However, as an after-thought, he said: "I guess my greatest problem is getting the people to bring their prescriptions to me after their physicians have instructed them to do so." I told him I would tell him just what was the trouble and exactly what to do to remedy the condition, if he promised me he would not throw me through the door. I asked him to step over to the main entrance, and I would show him his trouble. "My friend, perhaps you are so accustomed to your surroundings you cannot see things the way I do, but look over there to the lunch department; it is the first thing that greets the eye upon coming into the place. Do you honestly think if you, yourself, came in here to have a prescription compounded for your sick parent, wife or child, you would have it filled in this drug store? Personally, I would not.

I am quite sure if the appearance of your shop impresses me that way it is fairly possible others are affected likewise. I do not mean to criticize your lunch department, but if it were hidden from view of those in need of medical supplies, I am sure the medical supply and prescription departments would both be better off."

Another independent druggist of the mediocre type appeared to be very weary, worn and tired. He sauntered out from behind the counter at my approach. He was lean and long, needed a shave, although it was about 10:30 A.M., and was chewing on the stump of a cigar. "Well, what do you want?" I apologized for having disturbed him, made a small purchase and asked him: "How is business?" He answered, "Rotten," and he said it with a capital "R." I asked him what seemed to be his chief difficulty. To this he answered: "It's the competitive stores; they are hurting every one." I ventured a suggestion, asked him "if he ever tried hurting these stores?" He seemed surprised to think I had any idea that he could.—"Now here is my plan; first of all keep your store as neat as a pin; get rid of all those Gee Gaw cardboard signs; pile those magazines up in the corner, decorate the show-cases attractively, and then before I tell you the most important thing, I want to ask a question. 'Have you ever noticed the appearance of the competitive store clerks?' They are always young men just out of college, and they always wear those washable coats. Well now, 'you spruce up yourself, shave each morning and wear your regular street coat, the one which matches your trousers, retain a dignified appearance, and for heaven's sake take that stump of a cigar out of your mouth.' I could see he was about to boil over; I didn't blame him, you and I would also. The little reprimand may do some good; as a matter of fact I am going back sometime later to find out."

The next pharmacist I interviewed told me "his greatest problem was that he had to carry too varied a line of stock, trying to keep pace with each line." To make his long story short, he was never finished, but began each day where he left off on the previous one. Very foolish man; my suggestion to him was to get rid of some of the more irrelevant side-lines and cut down on some of his problems. I told him in plain words: "Don't try to sell everything. You cannot, because each and every other druggist is trying to do the same thing."

In closing, I would like to leave a thought with you, and that is: "Every man to his own activity." A piano tuner is not an electrician, nor is a pharmacist a merchant.

SELLING OF MEDICAMENTS IN FRANCE.

A French enactment of recent date relating to the hawking of medicaments and pharmaceutical products (*Bulletin de Pharmacie du Sud-Est*, 10, 1936) has a much wider application than its title suggests. It prohibits not only hawking, but also the sale of medicaments outside the pharmacy and of medicinal plants outside the pharmacy or herbalist's shop. There are three distinct provisions in the Act. *First*, the sale to the public of phylactic properties in any public place, in private houses or in any shops other than pharmacies, is strictly forbidden. *Second*, the sale of medicinal plants, mixed or simple, in any of the places mentioned, or in herbalists' shops, is prohibited. *Third*, it is illegal for pharmacists or herbalists to canvass the public for orders, either by representatives or agents or through order offices of a commercial character; to trade by such means; or to maintain regular and organized services to deliver goods ordered by such means.—(From *Chemist and Druggist*, 23/1/37.)

A PLEA FOR THE COLLECTION AND PRESERVATION OF STATE ASSOCIATION PROCEEDINGS.

BY EDWARD KREMERS.

In 1923 the then Chairman of the Section on Historical Pharmacy of the AMERICAN PHARMACEUTICAL ASSOCIATION planned a history of pharmacy in the United States.[1] He appointed thirteen chairmen of as many committees who, with such fellow committee men as they could induce to coöperate, were to write as many chapters of the history of our calling. A year later several chapters were handed in which, if I am correctly informed, are buried somewhere in the archives of the ASSOCIATION. After another year the Chairman whose committee was to prepare a history of our state associations complained that he could not induce the secretaries of our state organizations to coöperate. He had sent out a questionnaire but in most instances had not even received a reply. Far be it from me to blame the secretaries. Not only do I not believe in questionnaires, with very few possible exceptions, but I am certain that history, not even of that of our state associations will ever be written by preparing a summary of answers to a hundred questionnaires.

But, in coming before you, I do want to make a plea for the history of pharmacy in general and that of our state associations in particular. During the past few years, a number of golden anniversaries have been celebrated by state associations. More will be celebrated in the next few years. It is all well and good to publish an anniversary number even with golden letters, but something much more important is necessary if ever the history of state pharmaceutical associations is to be written by a competent historian some time in the future.

The first step in this direction should be taken by the secretaries of our state associations by developing in themselves a sense of responsibility for the preservation of organization documents, even if an historical sense is out of the question for the most part. I have reference particularly to the preservation of sets of proceedings of each state association. One would suppose that each secretary would regard this as one of his foremost duties. Yet such, I am sorry to state, is apparently not the case.

Inasmuch as changes occur in the office of secretary, the official of a given year may well blame his predecessor, and he in turn the one who preceeded him in office. This is pointed out not as an excuse but as an ameliorating circumstance. The situation having been what it was, the libraries of educational institutions, and occasionally other libraries, have stepped in to fill the breach. But this has been anything but a universal practice.

For a long lifetime the writer has made it his duty not only to secure complete sets of the Wisconsin Proceedings for the "General University Library," also for the "Frederick B. Power Pharmaceutical Library," the departmental library of duplicates, but he has made many efforts to secure the proceedings of other state associations. In this he has enjoyed the coöperation of staff members of the University Library. That they have been successful in a small measure is very gratifying and I herewith desire to thank all state association secretaries, past as well as

[1] JOUR. A. PH. A., 12, 183 (1923); 13, 69 (1924).

present, for their support. By way of illustration, permit me to report an experience or two. A number of years ago, a professor of pharmacy of a western university came to Wisconsin for a Summer Session. He had planned to spend one-half of his time in my laboratory and the other half in one of the chemical laboratories. It so happened that the first week of the Summer Session coincided with State Association week. So, after I had gotten him started on his problem, I suggested that he acquaint himself with the literature and spend several half days in the library while I was attending the annual meeting. He did. What is more, he spent the entire Summer Session in the library. Never before did he have such an opportunity to get first-hand information about the subject he was teaching. You may rest assured that I did not discourage him. During the next Summer Session he returned. The pharmacy professor of another institution spent a day in the city. After an hour spent together at luncheon, the three of us stepped over to the University Library across the street from the Club. While in the pharmacy stack, the resident professor told his migrating colleague how he had enjoyed the library facilities during the previous summer. "Why," he said, "I can find more here about my own state than in our own library." When we left, the other colleague remarked: "For years I have been wanting to do a certain piece of work. Now I know where to come to do it."

All of this is very gratifying, but it is only a part of my story. So far as state association proceedings are concerned our files are now relatively not as complete as they were then. During the past year the Assistant Librarian in charge of binding suggested that we make another effort to complete sets so that the annual brochures might be bound into volumes for greater safety and permanence. I was only too glad to promise my coöperation. I drafted a circular letter, a copy of which was sent to every association secretary. The Assistant Librarian added the list of proceedings wanted to complete our files.

Again, I want to thank those who coöperated. To the 48 personal letters sent out, seventeen replies were received. The net results were some twenty-five numbers of proceedings out of several hundred required to complete the sets. A rather poor showing. More discouraging, however, than the net results, is the apparent indifference on the part of most secretaries.

While the presidency of our state associations is occupied by a new incumbent almost every year, the secretary—even if he does not continue in office for a lifetime—is the relatively permanent officer of the organization. It should be his duty to act as archivist of all documents. Yet even of those who replied not a few reported that the secretary's office did not have a complete set of their own Proceedings. How a secretary can perform his duty in a satisfactory manner without a complete set of his own proceedings is beyond my comprehension. However, I am here not to tell you how to perform your secretarial duties, but to make a plea for the future historian of American pharmacy. As previously stated, it is perfectly proper for secretaries to get out anniversary numbers with gold letters or even with an entire gilt cover. But a collection of portraits of members, no matter how desirable, and the eulogistic remarks and reminiscences that are as common as proper on such occasions, are not history. Even the carefully collected newspaper clippings laboriously brought together as shown at the Madison meeting of the A. Ph. A. is not history, convenient as such a compilation will prove to the future

historian. We need critical papers based on documentary evidence not hearsay. These preliminary contributions cannot be prepared without complete sets of proceedings. It is for the preservation of these that I plead first of all. You, gentlemen, are duty bound to see to it that your respective state libraries are provided with such sets.

Lest my account seem pessimistic, permit me to close with a quotation from a letter received from the secretary of the Texas Pharmaceutical Association:

"A few years ago we attempted to get a complete file copy for ourselves and we were fortunate enough to locate some of these in your Library and some in Lloyd's Library at Cincinnati. We had typewritten copies made of these missing numbers and we hope some day to find the funds to have them reprinted. If this is ever done you may be sure that we will supply your library with a copy of the same as we feel deeply indebted to you for the service which you rendered us in this matter.

"We now have a complete copy of the Proceedings of each meeting or a newspaper account of the same. It is my opinion that probably one or two of the earlier meetings did not have a printed Proceedings and I resorted to old newspaper files for such information as I could get. I also was fortunate enough to secure photographs of all past-presidents and past-secretaries covering over 56 years. Very little of these records were in the files of the ASSOCIATION when I took hold of them thirteen years ago."

What Mr. Adams has done, each and every one of you can do if necessary. Far from being a pessimist, the very fact that I, a septuagenarian who soon must cease to do work of any kind, have asked for permission to make this plea to your body, must reveal to you that I am an optimist. Personally, I prefer to be neither pessimist nor optimist, but realist. So please see to it that what may seem visionary to many of you may become real.

PHARMACY IN THE UNITED STATES NAVY.*

BY E. G. SWANN.[1]

In the organization of every Navy ship there is a Medical Department and one of the units in this department is a dispensary, occupying a special compartment or room provided in the original construction plans of the ship. The built-in fixtures in this room consist of a prescription counter and cabinet, sink with hot and cold running distilled water, desk, file cabinet, narcotic and poison locker, book racks, shelves and bottle racks. The equipment consists of a prescription balance, sterilizer, refrigerator, electric hot plate, mortars and pestles, pill tile, shelf bottles, graduates and many minor items of equipment required in compounding and dispensing. The dispensary is stocked with all items of medical supplies listed on the Naval Medical Supply Table. The pharmaceutical library consists of a copy of each of the latest editions of the United States Pharmacopœia, the National Formulary, the Pharmaceutical Recipe Book, the United States Dispensatory, a textbook on the "Principles of Pharmacy" and a textbook on "General Chemistry." In addition there are available to all the Hospital Corps men the books and journals

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* Read before City of Washington Branch, A. PH. A., May 19, 1937.

[1] Chief Pharmacist, U. S. Navy.

in the medical and dental library of the ship. There are about seventy-five large and one hundred and twenty-five small dispensaries on Navy ships.

There are about forty dispensaries located in naval hospitals and at shore stations. These dispensaries are equipped with the usual fixtures and equipment found in a modern dispensary in a civil hospital. They are stocked with all the items of drugs on the Naval Medical Supply Table and additional items of drugs and preparations required for treatment of the sick. The Metric System of weights and measures is used exclusively in compounding and dispensing in the Navy. This practice is in accordance with an order approved by the Secretary of the Navy, dated April 15, 1878, which directs that "The Metric System of weights and measures shall hereafter be employed in the Medical Department of the Navy."

Forty-five preparations of United States Pharmacopœia and 49 National Formulary preparations are compounded and dispensed in the Navy from the stock of drugs and preparations listed on the Naval Medical Supply Table.

In addition to these United States Pharmacopœial and National Formulary preparations many of the preparations listed in the Pharmaceutical Recipe Book and special preparations are compounded and dispensed.

The medicinal substances listed on the Naval Medical Supply Table may be classified as follows:

124 U. S. Pharmacopœial drugs and chemicals
35 U. S. Pharmacopœial pharmaceutical preparations
7 National Formulary drugs and chemicals
4 National Formulary pharmaceutical preparations
12 U. S. Pharmacopœial biologicals
8 New and Nonofficial Remedies—biologicals
13 Other Nonofficial drugs and preparations
40 Reagent chemicals.

These make a total of 203 different medicinal substances, excluding the reagent chemicals, of which 150 are listed in the 1936 edition of "Useful Drugs." This tabulation shows clearly that the Navy uses principally official drugs and preparations in the treatment and prevention of disease. A few proprietary remedies are used such as Insulin, Protamine Insulin, some of the roentgenological diagnostic agents, the new organic arsenicals, etc., but the general policy is to use the proprietary drugs with discretion.

Medicines and all other medical supplies including surgical dressings, surgical instruments, dental supplies and X-ray supplies for the Navy are purchased, inspected, stored and distributed by the Naval Medical Supply Depot at Brooklyn, New York. This depot is equipped with chemical, physical, roentgenological and bacteriological laboratories where careful inspections are made on all materials purchased prior to their acceptance. The work in these laboratories is performed by members of the Hospital Corps under general supervision of medical officers. There is also a Naval Medical Supply depot located at Mare Island, California, and one in the Philippines, but all supplies are purchased by the depot in Brooklyn.

Pharmaceutical duties in the Navy are performed by members of the Hospital Corps under general supervision of medical officers.

In the early period of our naval history pharmaceutical duties in the Medical Department were performed by warrant officers known as surgeon's mates. The

duties of a surgeon's mate were outlined in detail in the Rules and Regulations for the Naval Service, 1818, as follows:

DUTIES OF THE SURGEON'S MATE.

"1. They shall be subject to the orders of the surgeon. They shall weigh or measure every article of medicine and hospital stores issued. They shall keep a journal of the diseases and treatment of all cases, an abstract of which shall be given to the surgeon, that he may be able to report thereon to the Secretary of the Navy at the expiration of every cruise.

"2. They shall be careful to see that the medicines prescribed are administered as directed and that the sick are supplied with proper nourishment. They shall be particularly careful in directing the loblolly boy to keep the cockpit clean, and every article therein belonging to the medical department. They shall, under the direction of the surgeon, personally apply dressings to wounds and ulcers, perform the operation of blood letting, and, in all important cases, they are personally to administer the medicines prescribed or see them given, and do all other duties appertaining to their profession which the surgeon may direct.

"3. They must direct the orderlies to wash all bandages and compresses daily in hot water with soap or potash and see that they are returned clean and dry to the cockpit.

"4. In the absence of the surgeon the mate eldest in commission shall act as the surgeon. They shall likewise aid in preparing the necessary reports required by the rules and regulations of the Navy."

The title "Surgeon's Mate" was superseded by the title "Surgeon's Steward" some time after the year 1828. A Circular Order of the Navy Department dated April 1, 1841, referring to surgeon's steward reads in part as follows:

"A surgeon's steward is allowed at all hospitals and navy yards and on board every vessel having a medical officer. As it is important that a respectable class of persons should be employed in this capacity, surgeons will endeavor to select such as have some knowledge of pharmacy and ordinary accounts and are of industrious and temperate habits."

The title "Apothecary" superseded the title "Surgeon's Steward" in accordance with a Circular Order of the Navy dated December 8, 1866, and reads in part as follows:

"The designation of persons serving as surgeons' stewards is changed to that of apothecary, and they will be appointed for duty in the Medical Department of the Navy, ashore and afloat, in the same manner as surgeons' stewards having heretofore been appointed. Apothecaries of the first class will rank with boatswains and will receive $750.00 per annum."

Three years later, 1869, first-class apothecaries were reduced in rank from the status of a warrant officer to the status of a petty officer and continued in that status until the year 1898 when some of the senior ones were appointed warrant officers in the new Hospital Corps.

Apothecaries were appointed from civil life. They were supposed to have been representative men of the pharmaceutical profession of their time. The Naval Regulations in 1896–1898 restricted the enlistment of apothecaries in their first enlistment to graduates of recognized colleges of pharmacy between the ages of twenty-one and twenty-eight years. They were required to pass a professional examination before a board of three medical officers and to present testimonials or certificates as to character, good habits and sobriety.

The apothecary rating was abolished in the year 1898 when Congress passed an act creating the Hospital Corps. This act extablished the warrant grade of "Pharmacist" and the enlisted ratings of "Hospital Steward" and "Hospital Apprentice."

Twenty-five of the apothecaries were appointed to the new grade of "Pharmacist" and the other apothecaries were enlisted as hospital stewards and hospital apprentices. In the year 1912 Congress passed an act creating the grade of "Chief Pharmacist" to rank with, but after, ensign.

The present organization of the Hospital Corps is in accordance with an act of Congress passed in 1916. This act provided for one commissioned warrant grade, one warrant grade and six enlisted ratings designated by the following titles:

Chief Pharmacist (Commissioned Warrant Officer)
Pharmacist (Warrant Officer)
Chief Pharmacist's Mate (Chief Petty Officer)
Pharmacist's Mate First Class (First Class Petty Officer)
Pharmacist's Mate Second Class (Second Class Petty Officer)
Pharmacist's Mate Third Class (Third Class Petty Officer)
Hospital Apprentice First Class
Hospital Apprentice Second Class.

The training of Hospital Corps men is a subject of great importance and one to which the Bureau of Medicine and Surgery gives much serious consideration. During their first enlistment Hospital Corps men are given general training which includes a course at one of the hospital corps schools followed by practical and theoretical instruction in the naval hospitals and service on board ships. In order to provide adequate numbers of Hospital Corps men trained as technical assistants sixteen different courses are given to selected men who have finished four or more years of service. One of these is a course in pharmacy and chemistry given at the Naval Medical School, Washington, D. C. The purpose of this course is to train men for duty as pharmacy technicians in naval dispensaries, and for duty as chemistry technicians in the chemical laboratories of the Medical Department. It covers a period of nine months' theoretical and practical instruction, and while attending this course the students do not perform any other duty. Upon satisfactory completion of the course the men are awarded certificates as technicians in pharmacy and chemistry. The instruction is divided as follows: Chemistry 507 hours, pharmacy 773 hours, lectures 448 hours, laboratory work 832 hours. A number of selected officers and men are given courses in pharmacy and chemistry in universities at Government expense. Those receiving this special training work in the service laboratories and service schools.

Pharmaceutical training of all Hospital Corps men begins when they first enter the Navy. During the first four months' instruction at the Hospital Corps School they are taught weights and measures, simple pharmaceutical procedures, materia medica, toxicology and pharmaceutical arithmetic in addition to other subjects. In their advancement through the various ratings a higher degree of pharmaceutical knowledge is required for each successive step in promotion. Practical pharmacy is being taught daily in all of the dispensaries throughout the service.

Pharmaceutical duties constitute only a small part of the general duties of Hospital Corps men. They serve as general assistants to medical and dental officers in all their activities. Some of those in the warrant and commissioned warrant grades serve in various administrative positions such as appropriation accounting, property accounting, commissary supervision and personnel accounting.

THE DEPARTMENT OF THE AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY

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RUFUS A. LYMAN, *Chairman and Editor.* ZADA M. COOPER, *Secretary.*
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THE VISION OF any professional group must be an ever-expanding one if that profession hopes to hold a place in the world of service. Well does the writer remember when the field of pharmacy was looked upon as a one department field and a college of pharmacy as a one department college comparable to a "College of Chemistry." When the writer of this introduction first insisted that physiology was a basic pharmaceutical science he was dubbed as visionary and bordering on *dementia præcox*. It took a Commonwealth study to justify the position of physiology in the pharmaceutical group. Bacteriology was a later addition to the basic science group. It has had to feel its way in, in the form of one- or two- or three-hour lecture courses. The time has come when a druggist without a laboratory knowledge of bacteriology can easily be a menace to a community, for without that knowledge he can neither conduct a sanitary drug store nor appreciate the care that is necessary to preserve the potency of a multitude of instruments of precision that are necessary in the scientific treatment of disease. In the paper which follows, Dr. George Reddish has stated in a most convincing way the value of bacteriological knowledge to both the student and practitioner of pharmacy.—*The Editor.*

THE TEACHING OF BACTERIOLOGY TO PHARMACY STUDENTS.

BY GEORGE F. REDDISH.*

Bacteriology, as an independent subject, is a newcomer to the curriculum of many pharmacy schools. In some schools materia medica courses have in the past included some instruction in bacteriology and immunology, while in others short separate courses covering these subjects have been offered. In still others full courses in bacteriology have been given for a long time. With the general acceptance of the four-year course in pharmacy, more schools have recently added separate departments devoted to the teaching of bacteriology entirely. This recognition of the importance of this subject to pharmacy students and to pharmacists is another indication of the progress made by schools of pharmacy within recent years.

Whether bacteriology is as important to the pharmacist as chemistry, pharmacognosy, pharmacology and the various courses included under the general heading of pharmacy, is perhaps beside the point, but it is, nevertheless, a valuable addition to the pharmacy school curriculum. Students do obtain additional training in this course which enables them to become even better pharmacists than they would be without it. Many practicing pharmacists to-day recognize the need of more fundamental knowledge of this subject, and have encouraged the establishment of separate bacteriology departments in our pharmacy schools.

It will be of interest to discuss the teaching of bacteriology to pharmacy students in the light of its subsequent value to them as practicing pharmacists. It is not my intention to outline a course in bacteriology for pharmacy students, nor to attempt to state exactly how such a course should be taught. I shall confine myself to pointing out the value of bacteriology to the pharmacist with the suggestion

* St. Louis College of Pharmacy.

that such courses be designed to meet his needs. Teachers of bacteriology have their own methods of teaching this subject, but all of us should direct our efforts to the same end—to present the course in such a way that the pharmacist will reap the most possible benefit from the instruction given. In other words, instead of giving a general course in bacteriology, we should, as far as possible, give a course in pharmaceutical bacteriology. Instead of attempting to designate exactly how this should be done, I would prefer to point out the value of such instruction to the pharmacist with the suggestion that courses in bacteriology be planned accordingly.

In what different ways will instruction in bacteriology be valuable to the pharmacist in the practice of his profession? Having had a course in bacteriology, how is the pharmacy student better fitted to become a competent pharmacist—in what respects is he better equipped to establish himself as a member of this ancient and time-honored profession? In the first place, a course in bacteriology better equips the pharmacist to coöperate with the physician, the dentist and the veterinarian to a fuller extent than he could without such training. He is able to intelligently discuss bacteriological matters with members of these professions and often be of assistance to them. Because of the close relationship between these professions and pharmacists a certain interdependence has grown up between them which becomes stronger and closer as each understands the problems and difficulties of the other, with the result that they expect coöperation from each other. The members of these professions also have more respect for the pharmacists who display a fundamental knowledge of bacteriology and immunology and as a result of this added respect greater confidence in them naturally follows. This mutual respect between physician and pharmacist is of vital importance to both.

The course in bacteriology provides the pharmacist also with a broad knowledge of a subject which is becoming more and more important to him. This fundamental training first covers methods of growing and studying bacteria, their isolation in pure culture, identification and classification of representative non-pathogens, and pathogens, thorough study of the more important disease-producing bacteria and careful training in the special technique necessary in these studies. The use of various staining methods for identifying bacteria, demonstrating special and characteristic features, etc., are employed throughout the course. In addition, experience is obtained in the various sterilization procedures, in methods of making and sterilizing pharmaceutical solutions, etc. This fundamental training leads up to the special features of the course which are of most importance to practicing pharmacists.

Since the pharmacist by the very nature of his profession is concerned with the prevention and cure of disease—since he compounds prescriptions used for these purposes—he naturally is much interested in the actual cause of these diseases. Studying the cause of infectious diseases and their laboratory diagnosis constitutes one of the most important phases of the course in bacteriology. The laboratory diagnosis of many of these diseases is emphasized to such a degree that the student is competent, by the time he has finished the course, to make an accurate laboratory diagnosis of many of the more common infectious diseases. It is not expected that he will become an expert in these diagnostic procedures, but in an emergency or when a diagnostic laboratory is not available he can actually make these tests and obtain reliable results. While ordinarily the pharmacist is not asked to make these

diagnostic tests, and he should not be if a competent bacteriologist is available, there are times when he may be of assistance to the physician in this way. The fact that he is prepared to do so is important. The physician respects a pharmacist more because of this additional information and training in a subject allied to pharmacy. The pharmacist is for that reason more valuable, at least potentially, to the physicians whom he serves, as well as to his community.

While studying the fundamental characteristics of the bacteria which cause infectious diseases, full consideration is given to the factors concerned in the spread of disease. Methods of preventing disease—preventive medicine as it affects the public health as well as in its relation to the individual—are thoroughly studied. More important to the pharmacist, however, are the methods of preventing and treating diseases as applied to the individual. In this connection, a full understanding of vaccines and anti-sera is of prime importance. The fundamental nature of the various biological agents used for this purpose must be thoroughly understood. To do this requires first of all a comprehensive study of the methods used for making the various vaccines and biological sera. Along with a thorough understanding of the nature of these vaccines and sera together with the processes employed in making them, the student also obtains a clear conception of the manner in which they exert their activity, and how they are used. He learns the precautions which are necessary in the handling of these products, and why such care is so important. He also obtains a thorough understanding of standardization and dosage of these biologicals, as well as a better conception of the necessity for proper care on the part of the pharmacist in storing and handling these preparations. In addition the federal and state requirements as to labeling, dating, storage, etc., are thoroughly considered. As the result of careful training in this phase of bacteriology, the pharmacist is prepared to handle biologicals more intelligently and with more understanding.

In this connection full consideration is given the subject of immunity and resistance to disease—the natural defenses of the body against disease and how these can be maintained, and more particularly to methods for building up immunity. The general principles concerned with immunity, both natural and acquired, are studied in considerable detail. Those factors which are concerned with health and disease, with infection and resistance, with immunity, with diagnosis and treatment, with immunological agents in general, are all emphasized in their proper relationships. The value to the pharmacist of this part of the bacteriology course cannot be over-emphasized.

The use of germicides in preventing infection and the spread of disease is of much interest to the pharmacist. Since he handles a variety of such preparations—antiseptics and disinfectants—he should know the advantages and the disadvantages of the different compounds available for this purpose. In the treatment of this subject in the bacteriology course, due consideration must be given to laboratory methods of testing these preparations. It is important that this instruction be thorough and accurate. Because of misinformation relative to this subject in professional and lay literature, and even in some textbooks, it is all the more necessary that the teacher of pharmaceutical bacteriology keep up-to-date in this field. This is particularly so, because of the rapid changes taking place in this field due to the active research constantly being pursued, especially relative to antiseptics. In

addition to instruction as to the usefulness of the various classes of antiseptics and disinfectants, the pharmacy student must become acquainted with federal and state laws and regulations used in controlling these products. He must be taught to evaluate the label claims of such products and interpret the directions for use for the benefit of purchasers. Considering the importance of antiseptics and disinfectants in preventing infection and the spread of disease, the pharmacy student may expect to learn much of value regarding this subject in the bacteriology course.

Methods of controlling the sanitary quality of milk, water and food are studied from the standpoint of federal, state and municipal laws and regulations. While the pharmacist may not have occasion to actually make these laboratory tests, he should have an intelligent understanding of how they are performed, how they must be interpreted, and in general the value and significance of the various standards relating to these commodities. This part of the bacteriology course should be given the pharmacy student as though he were a potential health officer, because the pharmacist is in a position to exert an influence for good in the matter of assisting local as well as state and federal health officers in the sanitary control of these necessities, as well as encouraging the application of other sanitary measures for preserving the public health.

It is apparent from this brief survey that the pharmacist benefits in many ways from instruction in bacteriology. He not only is equipped to lend assistance to the physician, the dentist and the veterinarian in a number of ways, but because of his close contact with the public, he is in a position to disseminate good advice of a general nature which will be helpful to a clearer understanding on the part of the public of the constant menace of infection and disease through unsanitary practices, as well as to assist the public to an understanding of accepted methods of preventing infection and disease. He is also an influence for good in supporting the physician, the health officer, the local, state and federal authorities, in the promulgation and enforcement of laws and regulations for the promotion and protection of the public health.

It may not be amiss to mention another way in which the course in bacteriology is valuable to pharmacy students, and to potential pharmacists—training in the proper pronunciation and spelling of bacteriological terms. While this may seem of incidental importance, in my opinion it is of considerable consequence. I consider this so important that I devote the opening lecture each year to a discussion of this phase of the course. At that time I give a serious warning that throughout the course this feature will be emphasized, even to the extent of penalizing the student for incorrect usage and spelling in class quizzes, tests and examinations—at least during the first half of the course. It has been my experience that the student soon becomes so accustomed to the proper use and spelling of these technical terms that they become a part of his normal vocabulary.

The technical training obtained in courses in bacteriology is not only useful to pharmacists in the practice of their profession, but the general information derived from such courses has a cultural value which must not be overlooked. Pharmacy students and the pharmacists, while benefiting in large measure from the general information obtained from instruction in bacteriology, will profit most, of course, from the technical information and training which is presented.

PROGRAM, THIRTY-EIGHTH ANNUAL MEETING OF THE AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY.

Officers.

President, William G. Crockett; *Secretary-Treasurer*, Zada M. Cooper; *Chairman of the Executive Committee*, Ernest Little.

MONDAY, AUGUST 16TH.

9:00 A.M. Meeting of the Executive Committee.
9:00 A.M. Meeting of Teachers' Conferences.

CONFERENCE OF TEACHERS OF PHARMACY.

Officers.

Chairman, Charles O. Lee; *Vice-Chairman*, Elmer L. Hammond; *Secretary*, L. Wait Rising.

Program.

MONDAY, AUGUST 16TH, 9:00 A.M.

The Pharmacist Is More Than the Doctor's Cook, by Howard Stephenson.
Techniques in Library Research, by Dr. Carter Alexander.
And How Much Time to Prescriptions, by Dr. F. A. Gilfillan.
The Use of the Model Drug Store as an Academic Tool, by Professors Neal Bowman and John Lynch.

CONFERENCE OF TEACHERS OF CHEMISTRY.

Officers.

Chairman, Lewis C. Britt; *Secretary*, Justin L. Powers.

Program.

MONDAY, AUGUST 16TH, 9:00 A.M.

The Application of Objective Examinations in Elementary Organic Chemistry, Carl J. Klemme.
Are Delayed-Course Examinations Adaptable to Pharmaceutical Education? Charles H. Rogers.
Types of Examinations and Methods of Examining, James D. Russell.
Methods of Examining in Chemistry Pertaining to Pharmacy, Edward M. Altman.
Pharmaceutical Chemistry as Presented at the St. Louis College of Pharmacy, Thomas D. James.

CONFERENCE OF TEACHERS OF PHARMACOGNOSY AND PHARMACOLOGY.

Officers.

Chairman, Ralph D. Bienfang; *Secretary*, Forest J. Goodrich.

Program.

MONDAY, AUGUST 16TH, 9:00 A.M.

Laboratory Work in Pharmacology for the Pharmacy Student, A. Richard Bliss, Jr.
The Instruction of Advanced Students in Covering Scientific Literature, James M. Dille.
Experimental Pharmacology as a Teaching Tool, Arno Viehoever.
Pharmacology for Pharmacists, James C. Munch.
Predictive and Objective Examinations in Pharmacognosy and Pharmacology, B. V.Christensen.
Relationship of Botany and Pharmacognosy to Other Courses in Pharmacy, Wm. J. Bonisteel.
The Scope of Pharmacognosy Courses with Relation to Their Credit Value, C. C. Albers.
The Correlation of Working and Study Hours with Grades in Pharmacognosy, L. K. Darbaker.

Some Problems Arising in Teaching the Microscopy of the Powdered Endocrines, Marin S. Dunn.
The Pharmacognosy Institute at Zagreb University, Ralph Bienfang.
Biographical Notes on Teachers of Pharmacognosy, Autun Urgoc-Richard Wasicky, Carlos Stellfeld.
Report of Committee on Pharmacognosy of the National Research Council.

CONFERENCE OF TEACHERS OF PHARMACEUTICAL ECONOMICS.

Officers.

Chairman, W. Henry Rivard; *Secretary*, Ralph W. Clark.

Program.

MONDAY, AUGUST 16TH, 9:00 A.M.

Average Annual Earnings of Drug Store Employees Contrasted with Other Retail Employees, Frank A. Delgado.
An Exploration in Economics, after College What? W. Henry Rivard.
Nimble Dollar Fallacies, H. S. Noel.
Light and Architecture in Store Planning, A. L. Powell.
What Is Expected of a Drug Store Employee, Ralph W. Clark.
Others to be announced at the meeting.

SESSIONS OF THE ASSOCIATION.

FIRST SESSION, MONDAY, AUGUST 16TH, 1:30 P.M.

Roll Call.
Appointment of Committee on Resolutions.
Address of the President, William G. Crockett.
Report of the Secretary-Treasurer, Zada M. Cooper.
Report of the Executive Committee, Ernest Little.
Appointment of Nominating Committee.
Appointment of Auditing Committee.
Reports of Standing Committees:
Committee on Educational and Membership Standards, A. G. DuMez.
Committee on Curriculum and Teaching Methods, Henry M. Burlage.
Committee on Activities of Students and Alumni, Adolph Ziefle.
Delegates to the American Council on Education, Rufus A. Lyman.
Committee on Relation of Boards and Colleges, Hugh C. Muldoon.
Paper, Entrance Requirements, Charles B. Jordan.

MONDAY, AUGUST 16TH.

Annual Dinner, 6:00 P.M.
Address by Dean George Braxton Pegram.

SECOND SESSION, MONDAY, AUGUST 16TH, 8:00 P.M.

Reports of Standing Committees (*Continued*):
Committee on Libraries, Charles O. Lee.
Committee on Problems and Plans, Rufus A. Lyman.
Committee on Status of Pharmacists in the Government Service, A. G. DuMez.
Report of the Editor of the *American Journal of Pharmaceutical Education*, Rufus A. Lyman.
Reports of Special Committees:
Committee on Food and Drug Legislation, Charles B. Jordan.
Committee on Pharmacy Predictive and Achievement Tests, Carl J. Klemme.

JOINT SESSION OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, THE NATIONAL ASSOCIATION OF BOARDS OF PHARMACY AND THE AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY, TUESDAY, AUGUST 17TH, 9:00 A.M.

Report of the Fairchild Scholarship Committee, E. G. Eberle.
Report of the Committee on Pharmaceutical Syllabus, J. G. Beard.

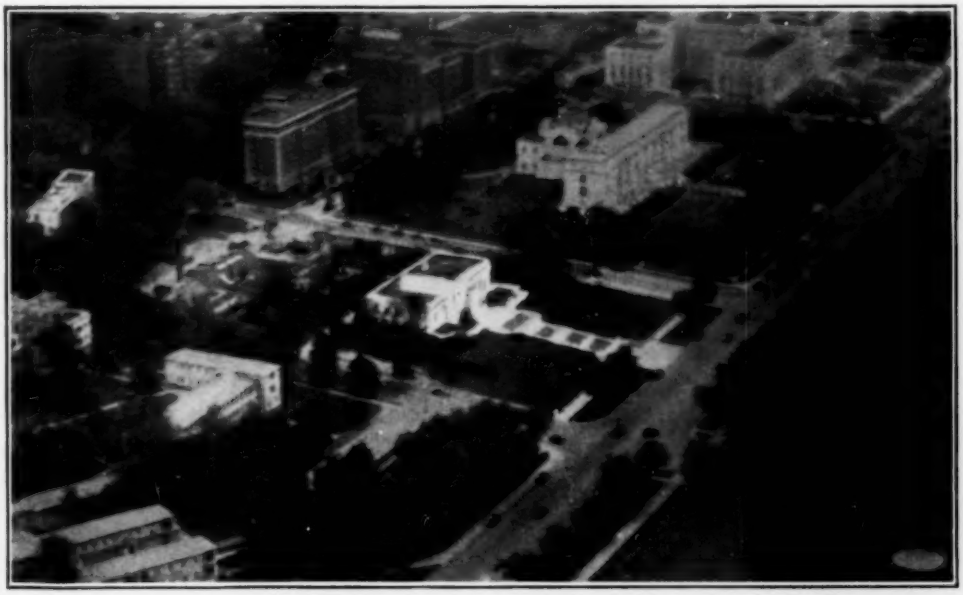
Report of the Council on Pharmaceutical Education, A. G. DuMez.
Report of the A. Ph. A. Committee on Development of Pharmacy Laws, R. L. Swain.
Report on Proposed Popular Publication, E. F. Kelly.
Report of Committee on Degrees, C. B. Jordan.
Paper, Recruiting for the Profession of Pharmacy, B. V. Christensen.

THIRD SESSION, TUESDAY, AUGUST 17TH, 1:30 P.M.

Reports of Special Committees (*Continued*):
- Committee on Professional Relations, George C. Schicks.
- Committee on Status of Women in Pharmacy, C. Leonard O'Connell.
- Committee on Time When Experience Can Be Secured to the Best Advantage, Charles B. Jordan.

Reports of Special Representatives:
- Representatives on the American Council on Pharmaceutical Education, A. G. DuMez.
- Reporter on Biological Abstracts, Heber W. Youngken.
- Representatives to the National Drug Trade Conference, A. G. DuMez.
- Representatives to the National Conference on Pharmaceutical Research, Franklin J. Bacon.
- Representatives to the Druggists Research Bureau, Paul C. Olsen.
- Representative to the National Association of Retail Druggists, C. Leonard O'Connell.

Report of the Historian, Edward Kremers.
Unfinished Business.
Miscellaneous.
Election of Officers.
New Business.
Executive Session.



A view from the air of the *American Institute of Pharmacy*. Presented by James G. Carstatter, Oneida, N. Y. Fronts on Constitution Avenue; opposite, not shown, is Lincoln Memorial. Left is Naval Hospital. On right, not distinct, Academy of Science, Public Health Service, Federal Reserve and Government buildings.

ASSOCIATION BUSINESS

AD INTERIM BUSINESS OF THE COUNCIL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 1936–1937.

Office of the Secretary, 2215 Constitution Avenue, Washington, D. C.

LETTER NO. 14.

June 9, 1937.

To the Members of the Council:

101. Use of Text of N. F. VI. Motion No. 47 (Council Letter No. 13, page 574) has been carried and Dr. Fischelis has been advised.

102. Election of Members. Motion No. 48 (Council Letter No. 13, page 574) has been carried and applicants for membership numbered 327 to 373, inclusive, are declared elected.

103. American Society for Testing Materials. Motion No. 49 (Council Letter No. 13, page 575) has been carried and the application for membership has been forwarded. The A. PH. A. has been advised that the organization meeting of Committee C-14 on Glass and Glass Products will be held in New York City on June 30th, and President Beal has requested Secretary Kelly to represent the A. PH. A. in the A. S. T. M., at this meeting. Later, a permanent representative will be appointed to serve on Committee C-14.

104. Laboratory in the American Institute of Pharmacy. One of the three activities to be established in the headquarters building as soon as practicable is a research laboratory devoted to the improvement and extension of official standards for drugs and medicines, the others being a reference library and an historical museum, and space was provided for such a laboratory in the building.

In the report of the Committee on National Formulary to the Council during the last annual meeting, in Dallas (see Item 181, A. PH. A. JOURNAL, Sept. 1936, page 805), Chairman Gathercoal discussed the personnel and activities of the N. F. Laboratory which was instituted on January 1, 1936, in space made available at the School of Pharmacy, University of Illinois, under his direction, and recommended "that definite action be taken by the Council to organize the A. PH. A. Laboratory in the A. PH. A. building at Washington and to transfer the present N. F. Laboratory into this larger project just as soon as possible." This recommendation was, after discussion, approved by the Council with the understanding that the transfer should be made as early in 1938 as was found to be possible.

In the meantime, further consideration has been given to the proposal by Chairman Gathercoal and by President Beal and other officers of the ASSOCIATION. Chairman Gathercoal, President Beal and Secretary Kelly met in Pittsburgh on June 7th, and carefully reviewed the developments to date in respect to the proposal. Through the coöperation of the A. PH. A. Committee on Maintenance, a supporting fund for the laboratory has been made available, over a trial period of three years, to supplement the funds now appropriated to the Committee on National Formulary, of a sufficient amount to justify proceeding with a study of the equipment of the laboratory, the personnel required and the work to be undertaken. It seems advisable to have this study undertaken promptly with the object of having rather definite plans submitted to the Council for consideration and action at the New York meeting in August, when they can be given personal attention.

(*Motion No. 50*) It is moved by Swain that a special committee of the Council consisting of Chairman Gathercoal, President Beal, Chairman Cook, Dr. Joseph Rosin and Dr. J. C. Krantz, Jr., with Chairman of the Council Hilton and Secretary Kelly as exofficio members, be authorized to make a study of the equipment of the proposed laboratory, the personnel required and the work to be undertaken, and to submit a report with recommendations, including a suggested budget of receipts and expenditures for 1938, to the Council at its first meeting during the New York meeting of the ASSOCIATION in August.

A vote on the motion is called for at this time since it is necessary for the Committee to undertake the study as promptly as possible, but it will be considered as tentative if there is objection or if members of the Council desire to submit comments.

105. Applicants for Membership. The following applications, properly endorsed and accompanied with the first year's dues, have been received:

No. 374, Calvin Berger, 1443 Sixth Ave., New York, N. Y.; No. 375, Werner M. Lauter, 195 Exchange St., Rochester, N. Y.; No. 376, Sam S. Dworkin, 358 E. 204th St., New York, N. Y.; No. 377, Edward David Mayo, 301 Henrietta St., Kalamazoo, Mich.; No. 378, Carl Alexander Abend, Grace Hospital, Detroit, Mich.; No. 379, George Thomas Griggs, Blodgett Memorial Hospital, Grand Rapids, Mich.; No. 380, Nathan Weiswasser, 320 Sterling St., Brooklyn, N. Y.; No. 381, Roger F. Eastman, 3019 N. 50th St., Omaha, Nebr.; No. 382, Benjamin Silver, 55 N. Swan St., Albany, N. Y., No. 383, Nathan Shalit, 27 Cutler St., Morristown, N. J.; No. 384, William J. White, 1110 DeVictor Place, Pittsburgh, Pa.; No. 385, Joseph B. Zubrick, 212 S. McKean Ave., Donora, Pa.; No. 386, Michael J. Derrig, Ridge Ave., Rankin, Pa.; No. 387, Albert N. Bohrer, West Plains, Mo.; No. 388, Susan Baratta, 1243 84th St., Brooklyn, N. Y.

(*Motion No. 51*) Vote on applications for membership in the AMERICAN PHARMACEUTICAL ASSOCIATION.

E. F. KELLY, *Secretary.*

LETTER NO. 15.

June 18, 1937.

To the Members of the Council:

106. Laboratory in the American Institute of Pharmacy. Motion No. 50 (Council Letter No. 14, preceding) has been carried and the members of the special committee are being notified. Dr. Gathercoal will serve as chairman of the committee.

107. Election of Members. Motion No. 51 (Council Letter No. 14, preceding) has been carried and applicants for membership numbered 375 to 388, inclusive, are declared elected.

108. Use of Text of N. F. VI. The following communication has been received from Chairman DuMez of the Committee on Publications:

"In response to the request of the Chicago Medical Book Company of recent date, it is recommended that that company be given permission to quote portions of the text of the N. F. VI in a new edition of Gray's 'Pharmaceutical Quiz Compend' and that the usual charge of $5.00 be made for this grant."

(*Motion No. 52*) It is moved by DuMez that the Chicago Medical Book Company be granted permission to quote portions of the text of the N. F. VI in a new edition of Gray's "Pharmaceutical Quiz Compend" with the usual acknowledgment and the customary fee of $5.00.

109. Proposed Publication. After consideration of the publication by the Council at its meeting in Washington on December 5, 1935, a Committee on Ways and Means, to study the financing, and a Committee on Contents, Scope and Style, to study the character of the proposed publication, were authorized (Council Letter No. 10, 1935–1936, Item 60).

The Committee on Contents, Scope and Style submitted its report to the Council at its first meeting in Dallas (Council Letter No. 28, 1935–1936, Item 182) and the report was referred to the conference on Pharmaceutical Association Secretaries, for consideration. The Conference returned the report with a communication (Council Letter No. 28, 1935–1936, Item 200), and the report and communication were received and referred to the Committee on Ways and Means, with the request that the report of the committee be submitted as promptly as possible.

It was expected that this report would be submitted to the Council at its meeting in Washington on December 7, 1936, but in the absence of Chairman Holton, no report was received (Council Letter No. 6, 1936–1937, Item 50).

Chairman Holton now advises that through the coöperation of the Committee on Maintenance, the amount estimated as necessary for the expenses of the proposed publication has been made available over a trial period of three years and suggests that the Committee on Publications be requested to review the proposal and to submit a report to the first meeting of the Council during the New York meeting of the ASSOCIATION including recommendations as to contents, scope and style, distribution, advertising, personnel required and a suggested budget for 1938, for consideration at that time.

(*Motion No. 53*) It is moved by Holton that the Committee on Publications be requested to submit a report with respect to the proposed publication to the first meeting of the Council

during the New York meeting including recommendations as to contents, scope and style, advertising, distribution, personnel required and a suggested budget of receipts and expenditures, for 1938 for consideration at that time, when it can be given personal attention.

Because of the necessity of prompt action, a vote on the motion is called for at this time but it will be considered as tentative if there is objection or if members of the Council wish to submit comments or suggestions.

110. Applicants for Membership. The following applications, properly endorsed and accompanied with the first year's dues, have been received:

No. 389, Allen Hopkins, Hopkins Drug Co., Carlisle, Ky.; No. 390, John Harper Albritton, 32nd & Bway., Paducah, Ky.; No. 391, F. E. Dunn, 1301 Park Ave., Paducah, Ky.; No. 392, Mary Frances Dunn, 1301 Park Ave., Paducah, Ky.; No. 393, Joseph C. Rogers, Barlow, Ky.; No. 394, James B. Overstreet, 2300 W. Oak, Louisville, Ky.; No. 395, L. R. Hugg, 12th & Monroe, Paducah, Ky.; No. 396, Wm. F. Reeb, 1114 Ash, Louisville, Ky.; No. 397, Robert Lee Lang, 213 Broadway, Paducah, Ky.; No. 398, Victor Mario Bianculli, 1407 Grotto St., Pittsburgh, Pa.; No. 399, Marcella Kunz, R. F. D. 4, Anderson Rd., Millvale, Pa.; No. 400, Karl Benjamin Hagmaier, 229 W. Pike St., Cannonsburg, Pa.; No. 401, Carroll Lyman Bryan, 428 Montview Pl., Wilkinsburg, Pa.; No. 402, Robert W. Newcomer, 1513 Blvd. Allies, Pittsburgh, Pa.; No. 403, Walter Wilbert Oehling, 33 Arlington Ave., Pittsburgh, Pa.; No. 404, Marion L. Jacobs, 208 North St., Chapel Hill, N. C.; No. 405, Dwight A. Joslyn, 41 Glendale, Detroit, Mich.; No. 406, Lily Betty Checkla, 6142 Kenwood, Kansas City, Mo.; No. 407, John Wilfred Courtney, Jr., University Drug Store, Charlottesville, Va.; No. 408, William Otto Krause, 203 E. E St., Belleville, Ill.

(*Motion No. 54*) Vote on applications for membership in the AMERICAN PHARMACEUTICAL ASSOCIATION.

E. F. KELLY, *Secretary.*

TWENTY-FIFTH ANNIVERSARY OF THE INTERNATIONAL PHARMACEUTICAL FEDERATION.

The International Pharmaceutical Federation held its first meeting in 1908. The president of the organization from 1912 to 1931 was Professor L. Van Itallie; he was succeeded by Dr. J. J. Hofman. The purpose of the organization is international coöperation. The AMERICAN PHARMACEUTICAL ASSOCIATION holds membership in the Federation.

On July 16th, Dr. J. J. Hofman commemorated his 50th year as a pharmacist and in view of this anniversary, several members of the "Netherlands Association for the Advancement of Pharmacy" formed a committee for the purpose of rendering homage to Dr. Hofman.

At the Congress of Brussels in 1910, Dr. Hofman, with the collaboration of M. R. Schoepp, presented a report entitled: "On the Formation of an International Association of Professional Pharmaceutical Societies."

Subsequently Mr. Hofman became secretary of the Provisional Committee and in 1912 was elected secretary general of the International Pharmaceutical Federation.

VISITORS FROM ABROAD.

Dr. Kurt Feinstein, of the Victoria-Apotheke Zürich—the "English Pharmacy," has recently completed a comprehensive article on "Percolation," its history and development, covering about 170 pages. It is well illustrated and presents researches at the Institute in Zürich. The author acknowledges the help of Dr. R. Eder, who visited in this country several years ago; of Professor Büchi and Apotheker Dr. H. A. Spangler.

He hopes to attend the New York meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION.

Another visitor who will attend is **Dr. George Urdang,** an honorary member of the A. PH. A.

President Thomas Marns, of the British Pharmaceutical Society, will visit the United States this year and it is hoped that he will arrange attendance at the New York meeting. He was a visitor at the Toronto convention.

E. N. Meusser, head of the Department of of Pharmacy, College of Science, West China, Union University advises that a pharmacy building is contemplated. Dean Meusser has been granted a year's furlough, which he will spend in Canada and the United States, reaching here about July 1st.

SCIENTIFIC EXHIBIT OF THE AMERICAN PHARMACEUTICAL ASSOCIATION AT THE CONVENTION OF THE AMERICAN DENTAL ASSOCIATION.*

BY GEORGE C. SCHICKS.[1]

The dentist is expert in the use of instruments for the treatment of diseased conditions of the teeth and the oral cavity. The use of medication should also be looked upon by the dentist as a most valuable instrument in treating his patients. The dental patient should be just as much entitled to a prescription necessitated because of dental treatment as is the patient of the physician.

Comfort during treatment of diseased conditions is greatly desired by the dental patient, although in many cases dentists feel that discomfort is a necessary accompaniment to treatment. Perhaps one of the greatest advertising possibilities the dentist has at his command is through the word of his patients who tell others that his treatment is painless.

Dentists for many years have prescribed drugs, but it has been the rare exception where the drug has been ordered through the medium of the prescription. Instead, dentists have employed the use of proprietary medication or merely suggested that the patient purchase the regular size of a sample which the dentist distributes. Such practices do not build up the scientific prestige which professional men so cherish. Being adept at mechanical dentistry is one important field, but the intelligent use of scientifically sound medicaments to treat existing pathological conditions as well as the field of preventive dentistry is of equal importance.

Can professional prestige be built up by a verbal word to the patient to go to the corner drug store and buy a package of a product sponsored on the favorite radio program? If a patient is not willing to accept the empirical treatment urged through magazines, radio or newspapers, and comes to the dentist because he wants specific treatment for his particular condition, isn't it a professional necessity that the dentist be professional in the medication he prescribes? Is not the professional use of scientific, sound medication an essential if further professional prestige is sought for the practice of dentistry?

The prescription is the most professional, intelligent and adaptable manner in which to prescribe drugs. It is the most intelligent because the dentist knows every ingredient in prescribing. It is the most adaptable because varying quantities of individual drugs can be employed to meet the varying pathological conditions of individuals as well as the varying degrees of the same pathological condition. It is the most professional, because it is a signed order by the dentist to the pharmacist. The number of refills can be controlled, the length of time the patient uses the medicament can be controlled, and the patient has a double check on the medication prescribed—a check by the dentist and a check by the pharmacist.

Never before in the history of medication have medicaments been so pleasing to the eye, so palatable and so pleasant to take. The day of ugly looking preparations and nasty tasting medicines is past. The color, odor and taste can almost be completely controlled by the scientific knowledge of the pharmacist. Color, odor and taste should not only be taken into consideration when medication is prescribed for oral administration, but it should also be taken into consideration when the dentist applies medication to the oral cavity in his office practice. Many people abhor the taste of phenol, which is sometimes used for its germicidal properties. If liquefied phenol is colored, and even flavored, it creates an altogether different psychological effect on the patient, who is so carefully watching every move and manipulation of the dentist. If the abrasive used in cleaning teeth is colored pink those patients who object to the sight of blood will be greatly relieved to find that the color they expectorate is the color of the abrasive rather than blood.

Children as well as adults prefer pleasant tasting abrasives, for the sandy sensation is greatly lessened if the flavor is pleasant. To the busy dentist these things may not mean much. The patient who looks upon the whole dental treatment from a different point of view greatly appreciates and often demands these finer points in dental treatment.

Whatever prescription writing the dentist has been taught he has obtained during his college course. In most cases very little time has been given to the consideration of this important subject. The Council on Dental Therapeutics makes available a very helpful publication to the

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* Atlantic City, New Jersey, July 12th–16th.

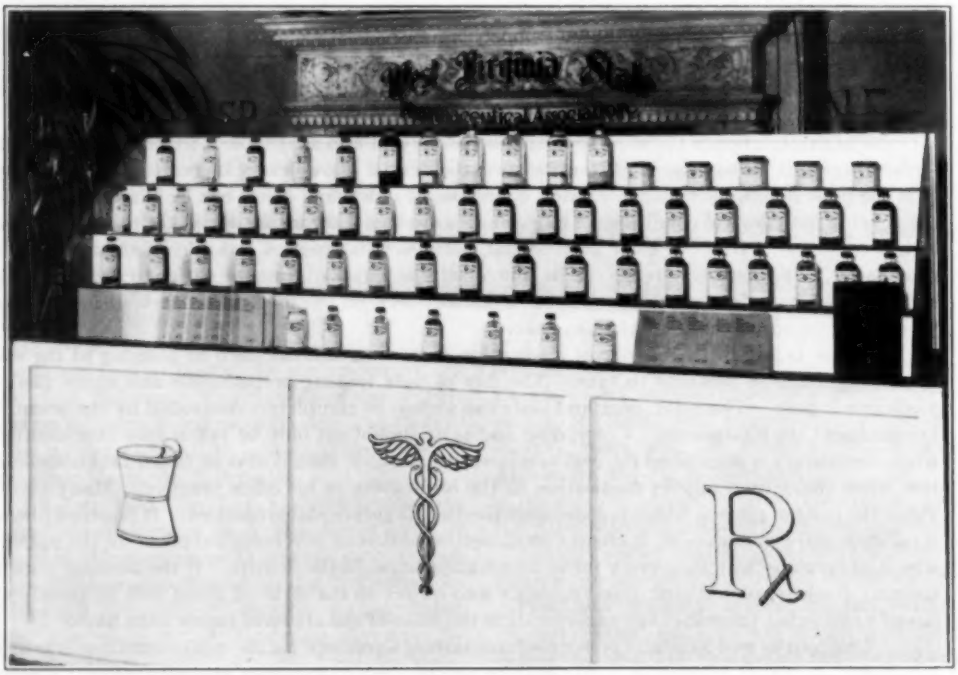
[1] Assistant Dean, Rutgers University, College of Pharmacy.

dentist in his prescription writing known as *Accepted Dental Remedies*. A copy of it should be in every dental office.

In addition to the service rendered by the dental colleges and the American Dental Association in making it easier for dentists to write prescriptions, colleges of pharmacy, through their specially trained staffs, are now coöperating with the dental profession by giving special lectures and demonstrations to the practicing dentists so that they may become more familiar with official drugs and preparations which are available for use in their practice.

Most medication which the dentist desires to prescribe can be found in either the United States Pharmacopœia or the National Formulary. These preparations are made of recognized therapeutic agents conforming to the highest standards. If the dentist is familiar with these official medicaments there will be no necessity to prescribe proprietary preparations.

The Scientific Exhibit of the AMERICAN PHARMACEUTICAL ASSOCIATION arranged by Rutgers University College of Pharmacy is designed to familiarize the dentist with the official drugs and preparations in the United States Pharmacopœia and National Formulary. This work supplements that of the Council on Dental Therapeutics, which is designed to familiarize the dentist with official medication entirely devoid of any proprietary application. Better medication means better satisfied patients and better satisfied patients mean a wider application of the national program of public health.



West Virginia Pharmaceutical Association U. S. P. and N. F. Display.

Prepare for the New York meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION.
For reference to programs, see second cover page.

CORRESPONDENCE

PHARMACY'S POSITION UNDER REGULATED COMMUNITY MEDICINE.

Dr. George Urdang, of Berlin-Wilmersdorf, Germany, *Honorary Member* of the AMERICAN PHARMACEUTICAL ASSOCIATION, replies to parts of the article by P. J. Callaghan, published in the April JOURNAL, pages 333–334, as they apply to Europe and, particularly, to Germany.

He states "that the first modern social security legislation was created in the latter part of the 19th century. It is not a fruit of socialism, but opposition—the intention of this legislation, as shown by the Imperial message of November 17, 1881, was to supersede the increasing socialism by an extensive official social care." The leaders of socialism gained very quickly decisive influence in the health insurance and in a relatively short time most of the officials of the largest and most important groups of the German health insurance bodies, of the "Ortskrankenkassen," were socialists. They tried to realize in these positions their political ideas and the drawback of generalizing the community medical treatment and especially medication, so often lamented, had here its origin.

"The statement, that the quality of medical care rendered under such systems is far below the average quality in this country, is only conditionally correct. Such practice was always more of a danger than a fact and it was only the exception and at no time a rule when a person with a serious ailment would go on the outside for treatment.

"Naturally in all countries having health insurance the physicians economize in prescribing for the insured."

Dr. Urdang refers to his book in collaboration with Dr. Adlung, "Compendium of the History of German Pharmacy," published in 1935. The authors listed restrictions on physicians' prescriptions, explained the relations of physicians and pharmacists, and possibilities of restrictions, proposed and tried. The following are given by Dr. Urdang:

"1. The doctor's obligation to prescribe only medicines or substances, listed in so-called 'Arzneiverordnungsbücher.'

"2. The delivering of medicines by departments of the local health insurance bodies.

"3. The establishment of own health insurance pharmacies or the partnership of health insurance bodies of private pharmacies.

"4. The establishment of own manufacturing establishments for preparing remedies for organizations.

"5. Terms of reference for economical prescribing.

"6. The liability of the physician for all remedy costs exceeding a fixed amount within a fixed time for every insurant.

"7. The obligation of the insurant to pay a fixed part of the costs of every prescription in order to interest the insurant in low remedy costs."

In further explanation Dr. Urdang states:

"The lists of medicines or substances allowed to be prescribed for insurants by the physicians, introduced only in Germany, were removed after 1933.

"The delivering of medicines by departments of the single local health insurance bodies has been introduced principally in Germany and in Austria. In both countries it has been restricted in the last few years. In Germany it always was confined to the so-called 'freigegebenen Arzneitmitteln,' *i. e.*, the remedies allowed by law for the sale in the free trade outside the pharmacies.

"Own health insurance pharmacies exist in Poland, some Baltic countries and in some parts (cantons) of Switzerland. In most European countries the establishment of such pharmacies is forbidden.

"The partnership of health insurance bodies in private pharmacies is generally illegal. It is according to the public protest demonstrations of the Belgian pharmaceutical association in Belgium. The pretended private owners of the pharmacies in question are often men of straw and in reality employees of the health insurance body. Similar conditions exist in Switzerland.

"The establishment of own establishments for preparing remedies and of organizations for wholesale have been tried in Germany and in Austria. In Germany these trials after long struggle between the pharmacists and the health insurance bodies became stigmatized and are more or less illegal. They were stopped entirely after 1933. In Austria the situation is not clear. There has

been created in the time of socialistic government an official institution in order to regulate the prices for medicines used for insurances, the so-called 'Heilmittelstelle.' This institution acts as manufacturer and as wholesaler.

"It is evident that the establishment of own pharmacies and even in connection with establishments for wholesale, by the health insurance bodies, is considered as pure socialism. The principal axiom of the socialism, the elimination of the private activities and the taking over by a community, is here realized.

"Terms of reference for economical prescribing have been introduced in several countries. In Germany they are obligatory and their transgression is punishable.

"The liability of physicians for all remedy-costs exceeding a fixed amount within a fixed time for every insurant and the obligation of the insurant to pay part in the remedy costs are legal in Germany.

"In England physicians and pharmacists are paid in round sums. The English pharmacist receives for every simple medicine 3 pence, for every compounded one 5 pence and, additionally the costs for the ingredients.

"Doubtless, there are many and partly incisive restrictions for the medical care within the European health insurance, some being a fact, some being a dangerous possibility. Only the one mentioned by Mr. Callaghan—the delivering of remedies by the physician, is not included. The statement 'that in the European plan medication is furnished by the physician' and 'the pharmacist is left entirely out of the picture' is not correct.'

"The functions of the physician and the pharmacist are, in the European health insurance, separated and so here is given a very important chance for the pharmacists in countries without such general separation.

"As an inquiry, organized by the pharmaceutical association of Switzerland, 1935, has shown, in Europe the full liberty of delivering of medicine by the physicians exists, excepting in some Swiss cantons, only in England. Here the introduction of national health insurance has not accepted the axiom of this liberty. Remedies for insurants in England are only delivered by pharmacists.

"The reason is evident and has the same validity in all countries of the world. A conflict between the physicians' duty and his profit is to be avoided. The physician should be interested exclusively in the treatment of the insurants and by no means in the profit for the medicine. In the United States the physicians have quite the same liberty of delivering medicine as their English colleagues.

"Pharmacy and its proper function, the providing of medicine, tend in the countries of the old European continent to more and more legal restrictions to larger liberty; in England and the United States, it is just the reverse. Should it not be possible that all of them learn from each other what to do and what not?

"The health insurance may as well be the ascent as the descent of professional pharmacy in the United States. What it will be, depends on the activity of the American pharmacists, on their professional integrity and recognition of all possibilities of this subject."

EDITOR'S NOTE: The editor has endeavored to present the views of Dr. Urdang and he acknowledges that he may not have interpreted all of the communication of Dr. Urdang correctly. The latter has communicated his views in a spirit of helpfulness and the valuable article by Mr. Callaghan shows the importance of the subject.

UNIVERSITY ANNIVERSARIES.

Heidelberg celebrated its five hundred and fiftieth anniversary recently, and on June 30th, of this year, the University of Göettingen celebrated its bicentennial. The latter institution has been a great influence during periods of development of pharmacy. A number of American pharmacists are alumni of the university.

The "*Deutsche Apotheker-Zeitung*" has been publishing a series of illustrated historical contributions on German pharmacies in German Museums. In an issue before us there are illustrations of pharmacies of about the 18th Century and earlier. They are from Braunschweig, Ulm, Nürnberg, Düsseldorf, München, Darmstadt. The editorship of these historical articles is under the direction of Dr. Fritz Ferchl, well known in the publication of the German Apotheker—Kalender.

LOCAL BRANCHES

CITY OF WASHINGTON.

The May meeting of the City of Washington Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held May 19th, in the assembly room of the AMERICAN INSTITUTE OF PHARMACY. President W. Paul Briggs presided.

The minutes of the previous meeting were read and approved.

Dr. E. G. Swann, Chief Pharmacist, United States Navy, was introduced by the president. He read a paper entitled "Pharmacy in the United States Navy." As the greater part of the paper follows, the abstract is omitted from the Secretary's Report.

During the discussion that followed, L. F. Kebler pointed out that at one time in the Navy, there was an Apothecary General in charge. No one seemed to know why this office was abolished.

On questioning Dr. Swann, it was brought out that Pharmacists in the Navy, especially on the smaller ships, have to perform duties similar to those of physicians and minor surgical operations.

The next speaker introduced was Harry Rosen, who read a paper on "History of Pharmacology." Dr. Rosen's paper proved very interesting. He traced the history of pharmacology by steps to the present day, explaining that pharmacology now holds a foremost part in medical science. A discussion of the paper followed.

The last speaker of the evening was Dr. Workman of the United States Public Health Service. Dr. Workman's subject was "Methods of Testing Biological Products."

Dr. Workman stated that all leading Nations have some laws governing biological products. The first laws governing these products were adopted for the District of Columbia, thereafter a Federal law was enacted. In the laws there are provisions for inspectors, mode of inspections and issuing of licenses. Before a license is issued the authorities must be satisfied that the licensee has the proper equipment and personnel. All biologicals must meet certain specifications—they must be sterile, the label must show the name of product, name and address of manufacturer, the license number and expiration date.

Dr. Workman's address was very well received.

Dr. Hilton moved that the secretary write a letter to Dr. Taylor wishing him a speedy recovery. Seconded and passed.

L. E. Warren gave a tentative program for the next meeting which will be on October 18th, and also an outline program for the next year. V. B. NORELLI, *Secretary.*

UNIVERSITY OF FLORIDA, STUDENT BRANCH, AMERICAN PHARMACEUTICAL ASSOCIATION.

The University of Florida Student Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION held a special meeting, Thursday, April 8, 1937, to discuss final plans for our trip to Eli Lilly and Company. President George R. Jones presided at the meeting.

The treasurer, Walter Griffin, reported that thirty-two pharmacy students had paid their transportation for the trip.

Dr. E. J. Ireland, who had been asked to act as faculty advisor and sponsor on the trip, presented the final arrangements, mentioning the different side trips that would be taken between Gainesville, Florida, and Indianapolis, Indiana. He advised that all be present at the hotel in Indianapolis, Sunday night, April 11th, so that any further arrangements could be presented for visiting Eli Lilly and Company on Monday and Tuesday, April 12th and 13th.

A rising vote of thanks was given to George G. Smith, Eli Lilly representative, for his valuable assistance in the arrangements of the trip. BUFORD L. WHITE, *Secretary.*

STUDENT BRANCH, FOR THE YEAR 1936–1937, STATE COLLEGE OF WASHINGTON, PULLMAN, WASHINGTON.

Abstracted from a report by Belle Wenz, Associate Professor of Pharmacy.

The officers serving for the year were: *President*, Leonard Zagelow; *First Vice-President*, Ted Stahlborn; *Second Vice-President*, Gail Howard; *Secretary and Treasurer*, Miss Belle Wenz; *Reporter*, Harold Freed.

The Membership Committee was composed of: Edward Meyer, *Chairman;* John Scheel, Maxine Gumz.

The organization sponsored an alumni breakfast held the morning of Homecoming, October 3rd, at the Golf Club House.

Many interesting speakers appeared on the program during the year. In addition, movies and slides were shown. President M. J. Grady, of the state Pharmaceutical Association, reviewed the progress of pharmacy in the last forty years. Claude Edgren of Colfax, Washington, spoke to the Student Branch on "Experience Teaches Many Lessons." "The Military Side of Pharmacy" was presented by Captain Cohen of the Military Department of the State College. He spoke of the new regulation passed by Congress last year. He explained the qualifications for an appointment, reviewed the commissioned offices available, including salary, promotions and other information.

Ralph Herbison appeared before the group on March 16th. His subject matter was "Biologicals."

The commercial side of pharmacy was brought to the Branch by Max White, who stressed the idea that the business side of the drug store is essential.—Three outstanding ways to make money are: to reduce expense, to increase volume and to sell more merchandise on which the profit is greater.

"The Service a Professional Pharmacy May Render" was the topic chosen by Ben Miller, when he gave an address on April 15th. He has had very fine training with the Hart and Dilatush Exclusive Prescription Store in Spokane.

Rather unusual, but most stimulating was the next speaker to appear before the Student Branch, Mrs. R. L. Harford. Her subject was, "It Is All in Knowing How." Her address was full of practical ideas and advice.

President Peter Brady, of the State Board of Pharmacy, spoke of the work that had been accomplished by the Board of Pharmacy this year. Mr. Harney spoke briefly and referred to the Bumauer-Frank scholarship of $50.00. The last speaker on the regular program was Paul Perkins, of Eli Lilly & Co.

The movies shown were very educational. One was given by the Owens-Illinois Glass Company. Ray Felt, representative for E. R. Squibb & Company, presented a talking picture to the Branch entitled "This Vitamin Business."

The *Pharmaceutical Echo*, the magazine edited by the Student Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION, was again published by the group. It is a very neat booklet, containing articles by the members of the Pharmacy faculty, students and alumni, showing the progress made not only in the profession but here in the school. Those on the *Echo* staff this year were: *Co-editors*, Creta Kidder and Takeo Torigoe. *Business Manager*, Ray Seaman. *Circulation Manager*, Edward Meyer; *Advertising Manager*, Harold Freed; *Assistant Advertising Manager*, Orion Furness.

The year-end banquet, which is always one of the happy social functions sponsored by the Branch, was held on May 29th. The speaker on the program was F. M. Keville, Northwest District Manager of Eli Lilly & Company. Guests were present from many parts of the Inland Empire. Dean P. H. Dirstine served as *Toastmaster*. Musical numbers were enjoyed by the group. The Seniors in the School of Pharmacy are guests of the association on this occasion, and a pleasant evening is spent together.

The officers for next year are: Harold Freed, *President;* Ray Seaman, *First Vice-President;* Creta Kidder, *Second Vice-President;* Miss Belle Wenz, *Secretary and Treasurer.*

LOCAL A. PH. A. BRANCHES.

Detroit Branch elected the following officers: *President*, Earl Soop; *First Vice-President*, Ernest Collins; *Second Vice-President*, Robert Church; *Secretary*, Bernard A. Bialk; *Treasurer*, Frederick F. Ingram.

Chairman, Program Committee: Dean Roland T. Lakey.

PHILADELPHIA BRANCH, A. PH. A.

The chairmen of the Philadelphia Branch, A. PH. A. are as follows: *Program*, Frank H. Eby; *Membership*, S. H. Kerlin; *Professional Relations*, E. Fullerton Cook; *Entertainment*, R. A. Wentworth; *Practical Pharmacy*, Ambrose W. Hunsberger.—ARTHUR K. LEBERKNIGHT, *Secretary.*

PROGRAMS.

(In order to expedite the completion of the JOURNAL, the programs are not in regular order, because some copies were necessarily belated—see notes elsewhere.)

SCIENTIFIC SECTION.

Officers.

Chairman, Glenn L. Jenkins; *First Vice-Chairman*, B. V. Christensen; *Second Vice-Chairman*, Justus C. Ward; *Secretary*, F. E. Bibbins; *Delegate to House of Delegates*, H. M. Burlage.

FIRST SESSION.

1. Chairman's Address, Glenn L. Jenkins.
2. Secretary's Report, F. E. Bibbins.
3. Committee Reports.

   Board of Review of Papers, F. E. Bibbins, *Chairman*.
   Committee on Monographs, E. E Swanson, *Chairman*.
   Committee to Coöperate with the National Conference on Pharmaceutical Research, Arthur Osol, *Chairman*.
   Special Committees.
4. Appointment of Nominating Committee.
5. General Business.
6. Papers.

   "The Extraction and Estimation of Alkaloids in Toxicological Analysis," by C. O. Wilson and L. W. Rising.
   "The Chemistry of Passiflora Incarnata," by Edwin J. Fellows and Clayton S. Smith.
   "Assay of Spirit of Camphor," by Samuel W. Goldstein and William F. Reindollar.
   "The Detection of CO in Medicinal O_2," by Frederick K. Bell and John C. Krantz, Jr.
   "A Further Study of the Assay of N_2O," by Frederick K. Bell, C. Jelleff Carr and John C. Krantz, Jr.
   "A Study of Assay Methods for Methylene Blue," by F. A. Maurina and Neulon Deahl.
   "Stability of Ipecac Preparations," by Samuel W. Goldstein.
   "Solubility and Hydrogen-Ion Concentration of Quinine Salts," by Frederick F. Johnson.
   "Stable Supersaturated Calcium Gluconate Solutions," by Glenn L. Jenkins.
   "A Rapid and Accurate Method for the Assay of Silver Proteinates," by Margaret C. Swisher.
   "The Preparation of Some 2,2,2-Trialkyl Ethanols," by Robb V. Rice, Glenn L. Jenkins and Fitzgerald Dunning.
   "Notes on the Stabilities of Atropine and Hyoscyamine in Solution," by H. H. Fricke and K. L. Kaufman.
   "Para-Aminobenzenesulfonamide. Notes on the Colorimetric Assay," by Asa N. Stevens and Edward J. Hughes.
   "The Solubility Behavior of Lyophile Gelatins," by L. F. Tice.
   "Solargentum Solutions—Stability on Aging," by F. N. Van Deripe, R. S. Konnerth and R. E. Schoetzow.
   "A Study of the Chemistry of Cascara Sagrada," by Melvin W. Green, C. G. King and George D. Beal. (Lantern.)
   "The Hydrolysis of Menthyl Acetate and Acetylized Peppermint Oil. II." by Lawrence H. Baldinger. (Presented by title.)
   "Phenolic Derivatives of *p*-Amino Benzoic Acid," by Abraham Taub.
   "A Study of the Factors Influencing the Stability of Liquor Magnesii Citratis U. S. P. XI," by George E. Crossen and Charles H. Rogers. (Lantern.)
   "Triethanolamine Salts of Fatty Acids," by George W. Fiero.
   "Alcohol Content of Extractive Preparations," by E. G. King, Louis Goldberg, R. K. Snyder and E. N. Gathercoal.
   "The Quantitative Determination of Volatile Oils in Vegetable Drugs," by Louis Goldberg, R. K. Snyder, E. H. Wirth and E. N. Gathercoal.

"The Assay of Neocincophen Tablets," by Urban Oakdale, R. K. Snyder and E. N. Gathercoal.

SECOND SESSION.

7. Papers.

"A Phytochemical Investigation of Trillium Erectum," by Donald C. Grove, Glenn L. Jenkins and Marvin R. Thompson.

"A Phytochemical Study of Ipomoea Pes-Caprae (L) Sweet," by Gustav E. Cwalina and Glenn L. Jenkins.

"The Application of Statistical Methods to Pharmaceutical Research. V. How Many Are Enough?" by J. C. Munch. (Lantern.)

"Cannabis Sativa. IV. Methods of Detection," by J. C. Munch and H. W. Mantz. (Lantern.)

"The Influence of p_H in the Bioassay of Aconite Preparations," by Frank A. Bellman and Marvin R. Thompson.

"Present Status of Aconite Research," by William J. Bonisteel. (Lantern.)

"Penetration of Drugs and Poisons through Normal and Pathological Skin and Mucous Membranes," by David I. Macht. (Lantern.)

"The U. S. P. XI Standard for Tincture Digitalis," by L. W. Rowe and H. W. Pfeifle. (Lantern.)

"The Potency of Erythrophleum Alkaloids," by K. K. Chen, C. C. Hargreaves and W. T. Winchester. (Lantern.)

"II. The Potency of Periplocymarin, Bufotalin and Desacetyl-Oleandrin (Desacetyl-Folinerin)," by K. K. Chen, R. C. Anderson and E. B. Robbins. (Lantern.)

"III. The Significance of Sugar Component in the Molecule of Cardiac Glycosides," by K. K. Chen, E. B. Robbins and H. Worth. (Lantern.)

"IV. Comparative Sensitivity of the Toad and the Frog to Cymarin and Coumingine," by K. K. Chen, C. C. Hargreaves and W. T. Winchester. (Lantern.)

"V. The Action of Cardiac Drugs upon the Chromatophores of Toads," by C. C. Hargreaves, W. T. Winchester and K. K. Chen. (Lantern.)

"A Pharmacological Study of Ustilago," by William H. Hunt and Marvin R. Thompson.

"The Dose-Response Relationship in the U. S. P. XI Parathyroid Assay," by Lloyd C. Miller. (Lantern.)

"Toxicity in the Leaves of Rhododendron Californicum, Hook.: I." by F. A. Gilfillan and Chieko Otsuki. (Presented by title.)

"Evaluation of Cathartics," by Arno Viehoever.

"Properties of Trichophyton Gypseum," by Fanchon Hart.

"A Pharmacognostic Study of *Crysanthemum Balsamita* L., var. *tanacetoides* Boiss., Together with a Study of Its Volatile Oil," by Ralph F. Voigt, Charles H. Rogers and Earl B. Fischer. (Lantern.)

"Observations on Three Louisiana Capsicums," by Heber W. Youngken. (Lantern.)

"Chemical and Clinical Aspects of Sodium Perborate Therapy," by L. L. Manchey and S. Lee.

"A Study of Datura Stramonium," by Frank H. Eby, Frederick Scholl and David J. Phillips.

"Liquor Antisepticus," by K. S. Howell, Louis Goldberg, R. K. Snyder and E. N. Gathercoal.

"Antiseptic Value and Pharmacology of an Improved Calomel Ointment," by E. E. Vicher, R. K. Snyder and E. N. Gathercoal.

THIRD SESSION.

8. Report of Committee on Ebert Prize, Marvin R. Thompson, *Chairman*.
9. Report of Nominating Committee.
10. Papers.

"Growth Promoting Substances in Plants" by William J. Bonisteel.

"Studies of Lecithin Soaps," by Saul Caspe and L. G. Hadjopoulos. (Lantern.)

"Toxicity of Propylene Glycol," by J. H. Weatherby and H. B. Haag. (Lantern.)
"A Modified Reddish Cup Technique for Evaluating the Germicidal Activity of Liquid Antiseptics," by Arthur H. Bryan.
"The Standardization of Ergot—A Comparison of Results Obtained by the Modified Smith Colorimetric, the Cock's Comb and the Broom and Clark Methods of Assay," by Asa N. Stevens. (Lantern.)
"Stability of Drugs," by Arno Viehoever.
"The Toxicity of Cyanides," by James C. Munch and Justus C. Ward. (Lantern.)
"Bio-Toxicology. I. Methods," by James C. Munch. (Lantern.)
"Bio-Toxicology. II. Animal Tests upon Volatile Substances," by James C. Munch. (Lantern.)
"The Effect of Certain Barbituric Acid Derivatives as Anesthetics in the Assay of Digitalis by the Cat Unit Method," by William E. Fry and Edward E. Swanson. (Lantern.)
"A Comparative Study of Two Short Acting Barbituric Acid Derivatives," by Edward E. Swanson and William E. Fry.
"A Series of Contributions to the Question of the Relation between Chemical Constitution and Local Anesthetic Activity. I," by W. A. Lott and W. G. Christiansen.
"A Series of Contributions to the Question of the Relation between Chemical Constitution and Local Anesthetic Activity. II," by W. A. Lott and W. G. Christiansen.
"Homologues of Cyclopropane-Methyl Cyclopropane," by W. A. Lott, W. G. Christiansen and L. F. Shackell.
"A Comparative Study of the Colorimetric Vitameter and Biological Tests for Vitamin A," by A. Black, R. D. Greene, H. L. Sassaman and C. Sabo. (Lantern.)
"A New Enteric Coating and a Laboratory Method for Its Control," by A. G. Worton, G. F. Kempf, P. L. Burrin and F. E. Bibbins. (Lantern.)
"A Critical Study of the Tannin-Bearing Galenicals," by S. W. Arnett and C. O. Lee.
"Drug Extraction. XIV. The Extraction of Podophyllum," by William J. Husa and Paul Fehder. (Lantern.)
"Drug Extraction. XV. A Study of Fractional Percolation," by William J. Husa and C. L. Huyck. (Lantern.)
"Drug Extraction. XVI. The Effect of the Form of the Percolator on the Efficiency of Extraction," by William J. Husa and C. L. Huyck. (Lantern.)
"Drug Extraction. XVII. Modified Repetition Diacolation," by William J. Husa and C. L. Huyck. (Lantern.)
"Drug Extraction. XVIII. Modified Diacolation," by William J. Husa and C. L. Huyck. (Lantern.)
"The Genuine Cardiac Glucosides," by Arthur Stoll. (Presented by title.)

11. Report of Committee on Chairman's Address.
12. New Business.
13. Unfinished Business.
14. Election and Installation of Officers.
15. Adjournment.

SECTION ON HISTORICAL PHARMACY.

Officers.—*Chairman*, Loyd E. Harris, School of Pharmacy, Norman, Okla.; *Secretary*, Edward J. Ireland, School of Pharmacy, Gainesville, Fla.; *Delegate to the House of Delegates*, Heber W. Youngken, Massachusetts College of Pharmacy, Boston, Mass.; *Historian*, E. G. Eberle, 2215 Constitution Ave., Washington, D. C.

A brief Memorial Meeting will be held during the Second General Session. These tributes may be extended during the sessions of the Section on Historical Interests.

HISTORICAL SECTION PROGRAM.

1. "Early American Pharmaceutical Inventions," Charles Whitebread, Assistant Curator, Division of Medicine, U. S. National Museum.

2. "The President of the First Convention Called to Formulate the United States Pharmacopœia—Dr. Samuel Latham Mitchill, 1764–1831," by Dr. Lyman Kebler.
3. "State Pharmaceutical History," Dr. Edward Kremers.
4. "The Unfortunate Drug Experiences of Dante Gabriel Rossetti," by Dr. David I. Macht, Baltimore, Md.
5. "The Story of the Soda Fountain," by Ina Griffith (Apache, Oklahoma), University of Oklahoma, Norman, Oklahoma.
6. "The Authorship of the First Lititz Pharmacopœia," by Dr. C. O. Lee, Purdue University.
7. "The International Pharmacopœia of 1885," by Edward H. Niles, Indianapolis College of Pharmacy.
8. "Dr. Wm. Beaumont—American Physiologist and Pharmacist," by Dr. Edward J. Ireland, School of Pharmacy, University of Florida.
9. "A Comparison between an Early Drug Catalogue and the United States Pharmacopœia," by Dr. Ralph W. Clark, University of Wisconsin.
10. "The History of the School of Pharmacy of the University of Florida." Compiled by Dr. B. V. Christensen, Director of the School of Pharmacy of the University of Florida.
11. "Linnæus—the King of Flowers," Commander Louis H. Roddis, U. S. Naval Hospital, Honolulu.

In addition, Dr. Feinstein and Dr. George Urdang have consented to send and deliver an address, respectively.

SECTION ON COMMERCIAL INTERESTS.

Officers: *Chairman*, R. T. Lakey; *Secretary*, Joseph H. Goodness; *Vice-Chairman*, and Delegate to the House of Delegates, Henry F. Hein.

FIRST SESSION, WEDNESDAY, AUGUST 18, 2:00 P.M.

1. Chairman's Address. R. T. Lakey.
2. Report of the Secretary.
3. Appointment of Committees.
4. Papers.
   - "Principal Causes of Low Profits in Drug Stores," Paul C. Olsen.
   - "Must a Pharmacist Be a Psychologist?" Alice-Esther Garvin.
   - "Taxation: Vertical *vs.* Horizontal," James C. Carstater.
   - "Influential Intangibles," Clarence M. Brown.
   - "Some Uses of Color in a Drug Store," George F. Archambault.
   - "The Importance of the Pharmacist's Allied Professional Services to the Community," John McDonnell.
   - "The Place of the Professional Display in a Drug Store," Medford M. Cooper.
   - "Advertising Professional Pharmacy," Joseph A. Ortolan.
   - "No One Wishes to See a Morgue," Charles Ely.

SECOND SESSION, FRIDAY, AUGUST 20, 2:00 P.M.

   - "Fair Trade, Past, Present," Samuel Shkolnik.
   - "On Twenty-Five Cigar Counters," Walter Chase.
   - "The Chain and Independent Drug Store Situation as Revealed by the Census of American Business," Frank A. Delgado.
   - "Law, Economics and Business in Buying a Drug Store," Joseph H. Goodness.
5. Discussions.
   - Is Mass Production of Prescription Specialties Determining the Types of Prescriptions the Druggist Fills?
   - Can We Consistently Sell Remedies for Self-Medication in the Light of Present Status of Medicine?
   - What Are the More Effective Means of Better Enforcement of Fair Trade Laws?

How May We Meet the Price Cutter without Cutting Price?
(Twenty-six other titles are available for discussion if time permits.)

6. Unfinished Business. New Business.
7. Reports of Committees.
8. Election and Installation of Officers.
9. Adjournment. (See also June JOURNAL, page 576.)

PLANT SCIENCE SEMINAR.

See page 572. The following are additional numbers of the program.

TUESDAY, AUGUST 10TH.

9–12 A.M. Meeting at Philadelphia College of Pharmacy and Science.

"Notes Concerning the Relative Toxicity of the Hallides of Lithium to Green Mold (Penicillium italicum)," Bernard Melkon.

"How to Retain the Leaves on Mounted Evergreen Specimens," L. F. Jones.

Address—Dr. Edgar T. Wherry, University of Pennsylvania.

2–5 P.M. Horticultural Hall, Fairmount Park, Valley Forge Park, Picnic Supper.

Evening Meeting, at P. C. P. & S.—Movies of Seminars of Other Years, presented by L. K. Darbaker and Others. Exchange of Plant Specimens.

WEDNESDAY, AUGUST 11TH.

Motor to DuPont's famous Longwood Gardens.

Visit to Kimble Glass Plant, Vineland, N. J.

Evening Meeting, Hotel Cumberland, Bridgeton. Discussion of histological and botanical terms, led by P. D. Carpenter, University of Illinois.

THURSDAY, AUGUST 12TH.

All day trip by auto to Cape May Point, Delaware Bay and Beach Flora, Lake Lilly, Cape May City and up the Jersey Coast along the ocean, through Wildwood, Avalon, Ocean City, Atlantic City. The group will break up into smaller units. A Steel Pier Party may be planned.

FRIDAY, AUGUST 13TH.

No scheduled program except for those who wish it. Reach New York City in time for National Conference of Pharmaceutical Research at 2:00 P.M., August 14th.

The foregoing program was arranged by Professors Dunn and Eby and Dr. E. L. Newcomb. Those desiring accommodations should confer with Dr. Marin Dunn at Philadelphia College of Pharmacy and Science.

CONFERENCE OF PHARMACEUTICAL LAW ENFORCEMENT OFFICIALS.

FIRST SESSION, MONDAY, AUGUST 16, 1937, 9:00 P.M.

SECOND SESSION, THURSDAY, AUGUST 19, 1937, 9:00 P.M.

1. Call to Order.
2. Remarks by Chairman, Robert L. Swain.
3. Report of Secretary, M. N. Ford.
4. Report of Finance Committee.
5. Appointment of Conference Committees.
6. Pharmacy Law Enforcement in the Following States:

   New Jersey—Robert P. Fischelis
   New Hampshire—George A. Moulton
   North Dakota—P. H. Costello
   West Virginia—Roy B. Cook

New York—George W. Mather
Mississippi—Lew Wallace
Maryland—Robert L. Swain
Connecticut—Hugh P. Beirne
Massachusetts—Charles W. King
Rhode Island—A. Norman LaSalle
Maine—Alfred P. Manson
Vermont—Fred D. Pierce
Virginia—A. L. I. Winne

7. The Public's Problem in Pharmacy Law Enforcement in Mississippi, Lew Wallace, Secretary, Mississippi State Board of Pharmacy.
8. An Attempt at More Adequate Regulation of One-Man Drug Stores in Virginia, A. L. I. Winne, Secretary, Virginia State Board of Pharmacy.
9. The Recent Indiana Supreme Court Decision, Albert C. Fritz, Secretary, Indiana State Board of Pharmacy.
10. What Is a Patent or Proprietary Medicine? Robert P. Fischelis, Secretary, New Jersey State Board of Pharmacy.
11. Significant Aspects of the Uniform State Narcotic Act, Robert L. Swain, Secretary, Maryland State Board of Pharmacy.
12. The Necessity for Educating the General Merchant Regarding the Requirements of the State Pharmacy Act, Edward J. Prochaska, Secretary, Minnesota State Board of Pharmacy.
13. Round Table Discussions:
    Administration of Minimum Equipment Law.
    Experiences under the Barbituric Acid Laws.
    Should Boards of Pharmacy Be Limited with Legislative Authority to Refuse Drug Store Permits on Grounds of Public Convenience?
    Should Boards of Pharmacy Be Empowered with the Enforcement of Laws Which Are Purely Economic as Contrasted with Those of a Public Health Character?
    Legislation of Interest to Enforcement Officials.

TENTATIVE PROGRAM OF THE SECTION ON PRACTICAL PHARMACY AND DISPENSING.

"Some Remarks Based upon a Prescription Ingredient Survey," Ralph W. Clark.

"Stability Studies on Certain U. S. P. Spirits," William F. Reindollar.

"A Study of Emulsions," Paul T. Rees.

"The Correction of Incompatibilities in Prescriptions. I," Herbert M. Webb, Wm. J. Husa.

"A Professional Dispensing Problem," W. D. Strother.

"Is the Pharmacist a Poor Merchant Because He Lacks Training in Accounting, Economics and Business Studies?" Ralph R. Kreuer.

"Some Observations on the Use of Objective Examinations in Pharmacy," Lyman D. Fonda.

"Socialized Medicine in Tampa," Frank L. Coniglio.

"A Modified—One, Two, Three Enema," Raymond J. Hansen.

"The Pharmacist and Parenteral Solutions," Sister Crescentia Wise.

"The Rôle of the Pharmacist in Connection with Public Health Work," Benjamin E. Holsendorf.

"Solution of Ferric Chloride Easily Prepared," C. O. Lee and F. J. LeBlanc.

"On Preparing Liquor Cresolis Saponatus," C. O. Lee.

"Hydrogenated Castor Oil in Ointments. Part II. Cosmetics," George W. Fiero and Laurence D. Lockie.

PAPERS TO BE PRESENTED AT THE MEETING OF THE SUB-SECTION ON HOSPITAL PHARMACY.

1. "Chairman's Address," Louis C. Zopf.
2. "The Earliest Hospitals," Eleanor Kiris.
3. "Production of Ointments at the Falk Clinic," Frank S. McGinnis.

4. "The Duke Hospital Pharmacy," I. T. Resmer.
5. "A Beginning Course in Hospital Dispensing," T. Elida Larson.
6. "Professional Opportunities Open to the Hospital Pharmacist," Charles O. McCullom.
7. "Pharmacist - Physician Relationship," Carl A. Abend.
8. "Medical Requirements of the Hospital Pharmacy," W. J. Stainsby, M.D.
9. (Title to Be Supplied), Dean Edward Spease.
10. "The Value of the Pharmacist to the Hospital," Oliver W. Young.
11. "Problems of the Hospital Pharmacy," S. W. Morrison.
12. "Pharmaceutical Coöperation with the Hospital Staff," Aaron Lichtin.
13. "Hospital Pharmacy's Opportunity," W. Wilson McNeary.

TENTATIVE PROGRAM OF PAPERS OF THE SECTION ON EDUCATION AND LEGISLATION, AMERICAN PHARMACEUTICAL ASSOCIATION.

(For officers, see Roster, page IX, July.)

"Educating the Physician and the Pharmacist Regarding Official Type of Prescriptions *Versus* the Proprietary Type," Frank A. Delgado.

"Physicians, Patients and Prescriptions," Chester I. Ulmer.

"Meaning.....?" Wilbur L. Scoville.

"Number of Graduates and Registered Pharmacists Necessary to Maintain the Professional Personnel at the Proper Level," E. F. Kelly.

"Recent Developments in the American Council on Education," Rufus A. Lyman.

"Medical Economics and Pharmacy," Roland T. Lakey.

"Motivating the Course in Materia Medica," Victor Lewitus.

"Laboratory Work in Drug Store Arrangement Courses," Joseph H. Goodness.

"The Necessity for a Specific Course in Bacteriology for Pharmacy Students," Fanchon Hart.

"A Course in Laboratory Glass Blowing in a College of Pharmacy Curriculum," Horace M. Carter.

"Are the Colleges of Pharmacy Fulfilling Their Duties When They Merely Prepare Graduates in Basic Sciences?" E. J. Parr, Michigan State Board of Pharmacy.

"Should the Certificate of Qualified Assistant Be Given by the Pharmacy Boards after 1937?" Ernest Little, Rutgers University.

"Uniform State Narcotic Acts," Robert L. Swain.

"The Value of Technician Training to the Pharmacist and Legislation Protecting Same," D. B. R. Johnson, University of Oklahoma.

"Working Conditions in Retail Pharmacy," Wortley F. Rudd, Virginia.

"The Problem of Aptitude Testing in Pharmaceutical Education," Samuel S. Liberman.

Title Not Chosen, Wm. A. Jarrett.

Title Not Chosen, H. C. Newton.

Title Not Chosen, Mac Childs.

Title to Be Given, Wilbur L. Scoville.

Since the foregoing was set, a number of titles and papers have come in—these additions will be published in the Official Program.—See also second cover page and page 684.

MARIHUANA BILL PASSED.

Marihuana Tax Bill (H. R. 6906) was passed by House and Senate. Occupational levy on producers was reduced and exemptions were provided relative to hemp fiber.

AMENDMENTS TO FOOD AND DRUG ACT.

H. R. 7913, introduced by Congressman Virgil Chapman, Kentucky, seeks to amend the Food and Drug Act of June 30, 1906. The bill was referred to the Committee on Interstate and Foreign Commerce.

D. C. NARCOTICS BILL.

Chairman Palmisano of the House District Committee, on July 24th, introduced a bill for narcotic control which has been recommended by the District Commissioners.

During the second session of the last Congress similar bills were introduced in the Senate and House. The Senate draft passed both House and Senate, but was amended in the House and Congress adjourned before Congress conferees could adjust the differences.

It is provided that certain specified narcotics shall not be sold except on prescriptions and defines who can prescribe.

EDITORIAL NOTES

THE OLDEST HOSPITAL IN AMERICA.

In an illustrated article on "The Hospital of Jesus of Nazareth in the City of Mexico," established in 1524, and still in use, Lieutenant Colonel Edgar Erskine Hume[1] describes this institution in *The Military Surgeon* for July 1937.

Liberty is taken in quoting from the article mentioned above:

"Cortes caused adequate medical care to be afforded the civil as well as military personnel.

"Never before or since has there been given to the world so vast a collection of remedies as those brought to Europe from America at the period soon after its discovery, and of these the greater part were obtained from the Aztecs. Besides quinine, there were added to man's weapons against disease: Canabis indica, cascara sagrada, chenopodium, coca, copal, chaparo, curare, damiana, condurango, Peruvian balsam, sabadilla, sarsaparilla, tolu balsam and vervain—to mention only a few of them."

Dr. Hume interestingly gives an historical account of hospitals established by Spain and also the hospitals of Mexico. Another paragraph again refers to the list of drugs used by the Aztecs and states that Hernandez learned from the Mexicans the names of more than 3000 plants used in therapeutic practice.

Cortez wrote the King of Spain, Emperor Charles V, relative to the City of Mexico, "in which there is a street set apart for the sale of herbs in which can be found every sort of root and medicinal herb which grows in the country. There are house-like apothecary shops where prepared medicines are sold as well as liquids, ointments and plasters." The great Botanical Garden of Moctezuma supplied the herbs which the physicians used in their practice. Cortez also advised the King that it would not be necessary to send physicians from Spain as they were well provided for in that respect."

REPRINTS.

We have received from **Dr. John C. Krantz, Jr.**, the following reprints:

"Etiology of Gall Stones," by Maurice Feldman, Samuel Morrison and John C. Krantz, Jr.

"The Effect of Brominated Ethylenes on the Perfused Leg Vessels of the Frog," by John C. Krantz, Jr., C. Jelleff Carr, Sylvan Forman and Wm. G. Harne.

"Studies in the Metabolism of Alkalinized Dextrose," by J. C. Krantz, Jr., Ruth Musser, C. Jelleff Carr, Frances Beck and T. Nelson Carey.

"Sugar Alcohols. VIII. The Oxidative Specificity of Acetobacter Suboxydans," by K. Pierre Dozois, C. Jelleff Carr and John C. Krantz, Jr.

"A Comparative Study of the Effect of Santonin, Isoartemisin and Santoninamine on the Blood Sugar Level of Rabbits," by Wm. Ellsworth Evans, Jr.

"The Preservative Capacity of Sodium Formaldehyde Sulfoxylate in Certain Medicinal Preparations," by John C. Krantz, Jr., C. Jelleff Carr and Ruth Musser.

"A Modified Quinhydrone Electrode for Tissues," by John C. Krantz, Jr., C. Jelleff Carr and Ruth Musser.

"Effect of Isoartemisin on the Circulatory System," by Wm. Ellsworth Evans, Jr.

Prof. Dr. H. Zörnig has favored the A. PH. A. with an Inaugural Dissertation by Ulrich Meyer—"A Contribution to the Pharmacognosy of the Umbelliferæ."

FURTHER SUBJECTS FOR DISCUSSION AT THE CONFERENCE OF PHARMACEUTICAL ASSOCIATION SECRETARIES.

Charles J. Clayton has submitted the following subjects for discussion at the forthcoming meeting of the Conference of Pharmaceutical Association Secretaries. Several lists of questions were published in the June JOURNAL, page 576. The additional subjects are:

1. Methods of Financing Fair Trade Administration.

2. Objections to Omnibus Contracts.

3. What Is the Most Practical Time for Starting the Morning Sessions at Our State Conventions?

4. What Experiences Have Our Members Had with "Professional" Sessions at the Annual Meetings?

5. How About Merchandising Demonstration Programs at Our State Conventions?

[1] The Lieutenant Colonel presented an interesting report on the 12th International Congress of Pharmacy—see pages 1113–1119, December JOURNAL A. PH. A., 1935.

AWARDS FOR EXHIBITS AT THE ATLANTIC CITY MEETING OF THE AMERICAN MEDICAL ASSOCIATION.

The report of the Committee on Awards for exhibits presented at the Atlantic City meeting is given in the *Journal of the American Medical Association*.

Among the exhibits receiving honorable mention was the one by Marvin R. Thompson, University of Maryland, on "ergot and its active principles."

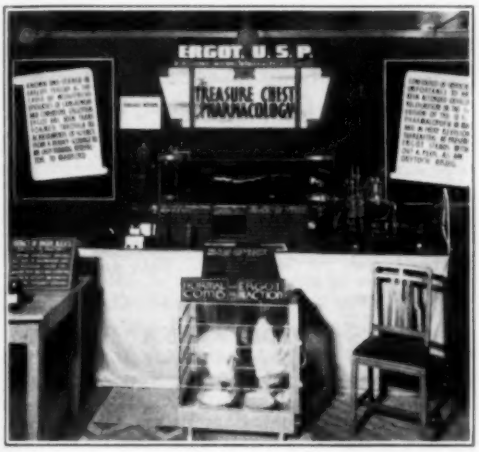


Fig. 1.—Marvin R. Thompson Exhibit at meeting of A. M. A. Front view. The exhibit involved a continuous demonstration of the various active principles of ergot.

Fig. 2.—Left end wall of booth, Thompson Exhibit.

THE ASSAY OF FLUIDEXTRACT of ERGOT. U.S.P. OR B.P. BY OFFICIAL METHODS..
10 YEARS OF U.S.P. XI REQUIREMENTS WITH ERGOTOXINE ETHANESULPHONATE AS THE STANDARD

Fig. 3.—Right end of wall of booth, Thompson Exhibit.

NEW AND NONOFFICIAL REMEDIES.

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.—PAUL NICHOLAS LEECH, *Secretary*.

ACETARSONE-ABBOTT (See New and Nonofficial Remedies, 1936, p. 90).

The following dosage forms have been accepted:

Tablets Acetarsone, 0.05 Gm.
Tablets, Acetarsone, 0.1 Gm.

TETANUS TOXOID, ALUM PRECIPITATED (See *J. A. M. A.*, May 16, 1936, p. 1735; Revised Supplement to New and Nonofficial Remedies, 1936, p. 16).

Eli Lilly and Company, Indianapolis, Ind.

Tetanus Toxoid, Alum Precipitated (Lilly).—Marketed in packages of two 0.5 cc. vials (one immunization treatment); and in packages of one 5 cc. vial (five immunization treatments).

CALCIUM GLUCONATE-ABBOTT (See *J. A. M. A.*, March 20, 1937, p. 973).

The following dosage form has been accepted:

Tablets Calcium Gluconate-Abbott (Flavored), 1 Gm. (15½ grains).

SALYRGAN (See New and Nonofficial Remedies, 1936, p. 308).

The following dosage form has been accepted:

Suppositories Salyrgan: Each suppository contains salyrgan 0.4 Gm., corn starch 0.1 Gm., and cocoa butter 1.3 Gm.

DEXTROSE (See New and Nonofficial Remedies, 1936, p. 290).

The following dosage forms have been accepted:

The Sterisol Ampoule Corporation, Long Island City, N. Y.

Sterisol Ampoule Dextrose 2½% in Physiological Solution of Sodium Chloride: A solution containing in each 100 cc. 2.5 Gm. of anhydrous dextrose and 0.85 Gm. of sodium chloride. Supplied in ampules containing 250, 500 and 1,000 cc.

Sterisol Ampoule Dextrose 10% in Physiological Solution of Sodium Chloride: A solution containing in each 100 cc. 10 Gm. of anhydrous dextrose and 0.85 Gm. of sodium chloride. Supplied in ampules containing 250, 500 and 1,000 cc.

Sterisol Ampoule Dextrose 20% in Physiological Solution of Sodium Chloride: A solution containing in each 100 cc. 20 Gm. of anhydrous dextrose and 0.85 Gm. of sodium chloride. Supplied in ampules containing 250, 500 and 1,000 cc.

Sterisol Ampoule Dextrose 25% in Physiological Solution of Sodium Chloride: A solution containing in each 100 cc. 25 Gm. of anhydrous dextrose and 0.85 Gm. of sodium chloride. Supplied in ampules containing 250, 500 and 1,000 cc.

Sterisol Ampoule Dextrose 5% in Distilled Water: A solution containing in each 100 cc. 5 Gm. of anhydrous dextrose. Supplied in ampules containing 250, 500 and 1,000 cc.

Sterisol Ampoule Dextrose 10% in Distilled Water: A solution containing in each 100 cc. 10 Gm. of anhydrous dextrose. Supplied in ampules containing 250, 500 and 1,000 cc.

Sterisol Ampoule Dextrose 20% in Distilled Water: A solution containing in each 100 cc. 20 Gm. of anhydrous dextrose. Supplied in ampules containing 250, 500 and 1,000 cc.

Sterisol Ampoule Dextrose 25% in Distilled Water: A solution containing in each 100 cc. 25 Gm. of anhydrous dextrose. Supplied in ampules containing 250, 500 and 1,000 cc.—From *J. A. M. A.*, May 15, 1937.

SYNTROPAN.—The phosphate of *d-1*-tropic acid ester of 3-diethylamino-2,2-dimethyl-1-propanol—$C_6H_5.CH(CH_2OH)COO.CH_2C(CH_3)_2CH_2N(C_2H_5)_2.H_3PO_4$.

Actions and Uses.—The actions of syntropan are similar to those of atropine. However, syntropan acts to a certain extent directly on smooth muscle in addition to its inhibitory effect on parasympathetic endings. It does not depress salivary secretion as actively as atropine or induce mydriasis as readily, and its inhibitory action on the parasympathetic innervation of the heart is not as pronounced as that of atropine. Syntropan is employed for its antispasmodic action on smooth muscle.

Dosage.—For oral administration, one tablet (50 mg.) three or four times a day; for subcutaneous or intramuscular administration, 1 cc. of syntropan solution (representing 10 mg. of syntropan) three times a day.

Manufactured by Hoffmann-LaRoche, Inc., Nutley, N. J. U. S. patents 1,932,341 (Oct. 24, 1933; expires 1950) and 1,987,546 (Jan. 8, 1935; expires 1952). U. S. trademark 308,080.

Ampuls Syntropan Solution, 0.01 Gm., 1 cc.

Tablets Syntropan, 0.05 Gm.

Syntropan occurs as a white, crystalline powder, with a faint roseate odor and having a bitter taste; freely soluble in water, slightly soluble in absolute alcohol, insoluble in chloroform and ether. The aqueous solution is acid to litmus. Syntropan melts at 142° to 145° C. From aqueous solutions, alkali hydroxides precipitate the free base as a water-white oil, which does not solidify at ordinary temperature.

Place about 0.01 Gm. of syntropan in a porcelain dish, add a few drops of nitric acid, and evaporate to dryness on a water bath: a yellow residue results; cool, add a few drops of alcoholic potassium hydroxide solution: the mixture is a violet color.

Dry about 0.5 Gm. of syntropan, accurately weighed, to constant weight at 100° C.: the loss in weight does not exceed 1 per cent. Incinerate about 0.5 Gm. of syntropan, accurately weighed, in a platinum crucible: the residue does not exceed 0.1 per cent. Transfer about 0.5 Gm. of syntropan to a 500 cc. Kjeldahl flask and determine the nitrogen content according to the official method described in Official and Tentative Methods of Analysis of the Association of Official Agricultural Chemists, third edition, page 20, chapter 2, paragraph 22: the percentage of nitrogen corresponds to not less than 3.3 per cent nor more than 3.6 per cent when calculated to the dried substance.—From *J. A. M. A.*, May 22, 1937.

NEO-IOPAX (See New and Nonofficial Remedies, 1936, p. 256).

The following dosage form has been accepted:

Ampoule Solution Neo-Iopax, 10 cc.: Each ampule contains neo-iopax, 7.5 Gm., dissolved in sufficient sterile distilled water to make 10 cc.

DEXTROSE (See New and Nonofficial Remedies, 1936, p. 289).

The following dosage forms have been accepted:

The Lakeside Laboratories, Inc., Milwaukee.

Ampules Dextrose (d-Glucose) 5 Gm., 10 cc.: Each ampule contains dextrose (*d*-glucose) 5 Gm., in distilled water to make 10 cc.

Sterile Solution Dextrose (d-Glucose) in Rubber Stoppered Vials 25 Gm., 50 cc.: Each ampule contains dextrose (*d*-glucose) 25 Gm., in distilled water to make 50 cc.

Sterile Solution Dextrose (d-Glucose) in Rubber Stoppered Vials, 50 Gm., 100 cc.: Each ampule contains dextrose (*d*-glucose) 50 Gm., in distilled water to make 100 cc.

TETANUS TOXOID, ALUM PRECIPITATED (See *J. A. M. A.*, May 16, 1936, p. 1735; Revised Supplement to New and Nonofficial Remedies, 1936, p. 16).

Mulford Biological Laboratories, Sharp & Dohme, Philadelphia and Baltimore.

Tetanus Toxoid, Alum Precipitated, Refined.—Marketed in packages of two 1 cc. vials (one immunization treatment); and in packages of one 10 cc. vial (five immunization treatments).

ANTIPNEUMOCOCCIC SERUM, TYPE II (See New and Nonofficial Remedies, 1936, p. 374).

The National Drug Co., Philadelphia.

Antipneumococcic Serum (Felton) Type II, Refined and Concentrated.—Prepared by immunizing horses with intravenous injections of virulent and avirulent pneumococci, and subcutaneous injections of the supernatant broth culture mediums in which the pneumococci had been grown. When test bleedings show the serum to have reached a sufficient degree of potency, the horses are bled aseptically and the serum is refined and concentrated by a method similar to that used for antitoxins. The potency of the product is determined and expressed in terms of the unit of Lloyd D. Felton. Marketed in packages containing 10,000 and 20,000 units of type II pneumococcus antibodies.

PHENOLSULFONPHTHALEIN (See New and Nonofficial Remedies, 1936, p. 194).

Phenolsulfonphthalein-"National."—A brand of phenolsulfonphthalein-U. S. P.

Manufactured by the National Aniline and Chemical Co., Inc., New York. No U. S. patent or trademark.

LIVER EXTRACT (INTRAMUSCULAR)-PARKE, DAVIS & CO. (See New and Nonofficial Remedies, 1936, p. 281).

The following dosage form has been accepted:

Solution Liver Extract (Intramuscular) P. D. & Co., 10 cc. vials.—From *J. A. M. A.*, June 12, 1937.

PERSONAL AND NEWS ITEMS.

Italy had in Africa, during the war period, 178 Army pharmacists and chemists, all officers, and 10 in the Navy.

John Russell Pope, architect of the AMERICAN INSTITUTE OF PHARMACY, designed the Tate Gallery, provided by Lord Duveen and dedicated by King George, June 28th, in London. A drawing by C. P. Eggers, architect, is shown in the *New York Times* for June 27th.

Dr. and Mrs. Malcolm T. MacEachern and daughter, Frances Isobel, sailed June 23rd, on the Queen Mary and met with the group of delegates from the American Hospital Association to the International Hospital Congress, in Paris.

Miss Margaret Cousins, former editor of the *Southern Pharmaceutical Journal,* is now with *Pictorial Review,* combined with *Delineator,* associated with **Herbert Mayes.** She is succeeded by her brother, **Walter Cousins, Jr.,** as associate editor.

Ralph Bienfang, of the Pharmacy Department, University of Oklahoma, conducts "Pharmacy Forum" of the Southern *Pharmaceutical Journal,* wherein questions on problems that trouble the readers are answered. The department is a valuable addition to the publication.

A bust of Dr. George Washington Carver, Chief of Chemistry at Tuskegee, and Director of State Department of Agricultural Research, was presented by friends to the Institution. Dr. Carver has been with Tuskegee for about forty years and tributes have been paid to him by various organizations for his outstanding work.

The American Association for the Advancement of Science at its Denver meeting made the first award of the Theobald Smith Prize of $1000.00 established by the Eli Lilly Company of Indianapolis. The award was made to Dr. Robley D. Evans, assistant professor of physics at the Massachusetts Institute of Technology, for his method of detecting radium poisoning.

Otto Raubenheimer's "Ye Old Herb Shoppe" is visited by patrons from New York City and from distant points.

S. L. Hilton has presented photographs of the present N. F. Committee, and of Committees of the fourth and fifth revisions.

Dr. Hilton also donated photographs of other groups and an analytical balance to the ASSOCIATION.

Dr. Irvin Abell, since 1904 professor of surgery at the University of Louisville, Kentucky, was made president-elect at the eighty-eighth annual meeting of the American Medical Association, held in Atlantic City from June 7th–11th.

Dr. A. John Schwarz, of the University of Tennessee, School of Pharmacy faculty, recently presided at the installation of Chi Chapter of Rho Chi at the University of Mississippi, of which the following are charter members: William J. Hossley, Jr., Toxey H. McBryde, George C. Furr, George C. Kealhofer, Clinton Kennedy Sample and Herbert E. Sumners.

J. G. Crownhart, secretary of the State Medical Society of Wisconsin in an address before Wisconsin Pharmaceutical Association, published in *Wisconsin Druggist,* stressed the importance of the pharmacist in public health service.

New Jersey Association has asked Dr. Robert P. Fischelis to continue his work as director of its research bureau which, in the absence of any state enforcement organization, requires compliance with the state fair trade law.

Wilber J. Teeters, dean of the College of Pharmacy at the University of Iowa since 1904, will retire on July 1st. He will be succeeded by **Prof. Rudolph A. Kuever.**

Dean Teeters, who will continue in the capacity of professor of pharmacy, joined the medical college of the university in 1895 and served there until 1903 when he became connected with the school of pharmacy.

Dean Charles W. Ballard, of Columbia University, College of Pharmacy, was honored by the teaching staff and other officials of Columbia University, College of Pharmacy, by a luncheon on July 1st.

Associate Dean Wimmer spoke for the guests and assured coöperation of his colleagues. Dean Ballard expressed appreciation of the coöperation.

Dean Howard C. Newton, of the Massachusetts College of Pharmacy, presented an address on "Careers in Pharmacy" at the convention of the Maine Pharmaceutical Association held at Mt. Kineo, June 21st, 22nd and 23rd.

Leslie M. Ohmart explained how druggists may profit by developing a dental prescription business.

SOCIETIES AND COLLEGES.

TEACHERS OF PHARMACY CONFERENCE.

Professor C. O. Lee advises that Dr. Carter Alexander, Library Professor, Teachers' College, Columbia University, will address the *Teachers of Pharmacy Conference* which is to be held during the week of August 16th in connection with the meetings of the American Association of Colleges of Pharmacy and the AMERICAN PHARMACEUTICAL ASSOCIATION. The exact time and place of this Conference will be announced in the program.

Dr. John C. Krantz, Jr., was recently elected president of the Maryland Chapter, American Chemical Society.

RECIPROCITY PLAN IN EXAMINATIONS.

The senior classes in ten colleges of pharmacy participated in the first District Examination conducted on May 3rd and 4th as an experiment to determine some of the underlying causes of the unsatisfactory showings made by pharmacy college graduates before examining Boards of various states.

Nine schools of District No. 2 and the University School of Pharmacy of Kansas took part in this examination.

Dean L. D. Havenhill was a speaker at the meeting of Kansas Pharmaceutical Association at which time he referred interestingly to the examination. It is hoped that all members of the Kansas Board of Pharmacy will be present at the New York meeting.

"DEAN EMERITUS" FRANKLIN T. GREEN.

The University of California Alumni Association and the Veteran Druggists' Association, of San Francisco, honored Frank Theodore Green with a banquet and testimonial at Elks Club, May 17th. An inscription to "A Gentleman—a Scholar and a Friend" paid tribute to the qualities of mind and character of the guest of honor.

More than 300 guests from all parts of California assembled, including a delegation from Southern California. The degree of *Dean Emeritus* was conferred by Vice-President Monroe F. Deutsch of the University of California. Director of Public Health, Dr. J. C. Geiger, representing Mayor Rossi Rossi, stressed the importance of professional pharmacy in its service to the public health of the community in his address paying tribute to the guest of honor.

A beautiful hand-designed parchment was signed by all present, as a testimony from the Veteran Druggists of San Francisco, of which organization Mr. Green has been the head for twelve years. Brief references to the latter may be found in the March JOURNAL, page 274.

A. B. LEMON.

A. B. Lemon has succeeded the late Dr. Willis G. Gregory, as dean of Buffalo University, College of Pharmacy. The senior class presented a plaque of the latter and the presentation was made with due ceremonies and addresses.

MISSISSIPPI U. S. P. AND N. F. PROGRAM.

The Mississippi State Board of Pharmacy, of which Charles E. Wilson of Corinth, Miss., is Director, is issuing interesting *Bulletins* relating to historical and professional pharmacy. In these bulletins various formulas are discussed, the purpose of the preparation, how dispensed and compounded. All of this matter is presented in a most interesting way in connection with the report of the U. S. P. and N. F. Committee. A very comprehensive annual report shows gratifying returns.

The success of this Extension work depends upon the physicians prescribing the official preparations. The bulletins are mailed to pharmacists several weeks in advance of the communication, addressed to the physicians, so that pharmacists can prepare for prescriptions included in the publicity.

Director Charles E. Wilson rendered his second annual report at the meeting of Mississippi Pharmaceutical Association at Biloxi. He reported that the mailing list of the committee had been increased to 872 names with 719 practicing physicians receiving the official bulletins and data. A display was made at the convention of the State Medical Society.

As an example of results, one pharmacist had compounded 152 prescriptions from one group outlined in the bulletins and 212, 78, 98 and 29 from other groups. The work is strictly educational and speaks well for the program being carried on by Mississippi.

The officers elected are: *President*, C. H. Hays, Philadelphia; *First Vice-President*, D. B. Sharon, Jackson; *Second Vice-President*, T. H. Spencer, Greenville; *Secretary-Treasurer*, S. B. Key, Jackson. The three immediate *past-presidents* include: S. J. McDuffie, J. S. Puller, Lew Wallace, who constitute the *Executive Committee*. The 1938 meeting will be held in Gulfport.

WEST VIRGINIA ASSOCIATION.

At the annual meeting of the Association *research* was declared to contribute great benefit to pharmacy by **President George D. Beal,** A. PH. A., because in addition to developing new products for the druggist's shelves "it is the best stimulant to teaching proficiency and professional pride that has ever been discovered. It interfuses ambition, zeal, spirit and self-satisfaction."

As speaker of the convention **R. L. Swain** declared that the statement "violates every conception of ethical treatment" is a mixture of suppressed truth, half truth and unjustifiable innuendo.

Charles V. Selby, secretary-treasurer of the Harrison County Retail Druggists' Association, spoke of the necessity of inducing physicians to write prescriptions instead of using products.

"Many of us lose sight of the fact that time spent in the perusal of drug publications can help us grow and that it can be made to pay dividends in our business," declared E. O. Wiseman of Fayetteville, retiring president of the association.

New officers are: *President*, G. S. Flesher, Cairo; *First Vice-President*, W. S. Coleman, Lewisburg; *Second Vice-President*, Harold J. Ridenour, Beckley; *Third Vice-President*, J. Edgar Johnson, Charleston; *Secretary-Treasurer*, J. Lester Hayman, Morgantown; Member of the Council, Robert R. Pierce, Morgantown. *Place of 1938 Meeting*, Charleston.

NOMINEES.

For *President*, W. S. Coleman, Lewisburg; C. G. Meadows, Logan.

For *First Vice-President*, Edgar B. Moore, Elkins; H. R. Ridenour, Beckley.

For *Second Vice-President*, Fred A. McFarlin, Clarksburg; and A. R. Johnson, South Charleston.

For *Third Vice-President*, L. L. Carson, Wellsburg; and Carl Walker, Gassaway.

For *Secretary-Treasurer*, J. Lester Hayman, Morgantown; S. M. Scott, Terra Alta.

For *Council Members*, E. O. Wiseman, Fayetteville; J. L. Jenkins, Charleston.

THIRD DISTRICT NATIONAL ASSOCIATION BOARDS OF PHARMACY.

A resolution recommending the appointment of Lew Wallace, of the Mississippi Board of Pharmacy, as chairman of the third district of the National Association of Boards of Pharmacy for the coming year was adopted at the third district's annual convention held in Charleston, S. C.

R. L. Crowe, of the College of Pharmacy of the University of Tennessee, was recommended for the secretaryship of the group.

Delegates attending the convention of the third district of Pharmacy, held jointly with the board meeting, recommended the appointment of Robert C. Wilson, dean of the College of Pharmacy of the University of Georgia, as chairman of the third district college group for the coming season.

Attended by delegates from seven southeastern states and Porto Rico, the joint meeting of the board and college groups was featured by discussion of proper courses of instruction in pharmacy and examinations of graduates for pharmacy certificates. Uniformity of requirement also came in for considerable discussion.

The group decided to hold next year's meeting in Athens, Ga., some time during April.

PENNSYLVANIA PHARMACEUTICAL ASSOCIATION.

J. B. Pilchard, secretary of Pennsylvania Pharmaceutical Association, has prepared a comprehensive abstract of the sessions of that organization held in Harrisburg, June 14th–17th. Among other interesting records reference is made to addresses, "Symposium on the Deterioration of Drugs," participated in by **James C. Munch,** *Chairman*, **Arthur Osol, Frank H. Eby, Herbert M. Cobe, H. B. Haag** and discussion by the members. An "Open Forum" was introduced by **Theodore Campbell, C. Leonard O'Connell, Leonard A. Seltzer, Ambrose Hunsberger, Jerome Abramson** and **John C. McDonnell.** Discussions followed the addresses of **Aaron Lichtin** and **Bernard Fantus.**

President De Haven's address included recommendations for more frequent meetings of pharmacists and physicians and the election of a vice-president to succeed as president, giving that officer more time to plan his year of office.

He discussed socialized medicine and pointed out its dangers.

The 1938 convention will be held in Wilkes-Barre, June 13th–16th.

CALIFORNIA ASSOCIATION.

California Pharmaceutical Association elected the following officers:

President, L. J. Fischl, Berkeley; *First Vice-President*, T. D. Perkins, San Diego; *Second Vice-President*, Charles Luedeking, Oakland; *Third Vice-President*, John G. Wagner, Long Beach; *Secretary*, Roy S. Warnack, Long Beach; *Treasurer*, Charles R. Seward, Pasadena. *Place of 1938 Meeting*, probably Oakland.

IDAHO ASSOCIATION.

Idaho Pharmaceutical Association elected the following officers:

President, J. Earl Evans, Idaho Falls; *First Vice-President*, C. C. Kingsbury, Twin Falls; *Second Vice-President*, E. W. Sinclair, Jerome; *Secretary-Treasurer*, Elmer B. Williams, Boise. *Place of Meeting*, Lewiston. *Time*, 1938.

NORTH DAKOTA ASSOCIATION.

The Nominating Committee brought in its report which is as follows: *President*, Earl Harding, Valley City, and H. W. Gray, Wilton; *Vice-President*, Dan Hall, Bismarck, and William Torgeson, Grand Forks; *Secretary*, Clarence Hay, Fargo, and Glen D. Shelver, Dunseith.

For the present year, 1937–1938, the officers of the Association are Philip H. Boise of Dickinson, *President;* H. W. Gray of Wilton, *Vice-President;* Clarence Hay of Fargo, *Secretary;* and P. H. Costello, Cooperstown, *Treasurer*.

SOUTH DAKOTA ASSOCIATION.

The following officers were elected by South Dakota Pharmaceutical Association for the coming year: *President*, Thomas K. Haggar, Sioux Falls; *First Vice-President*, C. A. Locke, Brookings; *Second Vice-President*, H. S. Crissman, Ipswich; *Third Vice-President*, J. A. Clute, Murdo; *Treasurer*, Frank S. Bockoven, Clark. *Place of 1938 Meeting*, Mobridge.

David F. Jones, of Watertown, acted as toastmaster at the South Dakota Pharmaceutical Association banquet.

UTAH ASSOCIATION.

Utah Pharmaceutical Association elected the following officers:

President, T. Ray Kingston, Murray; *First Vice-President*, Harold Voiles, Salt Lake City; *Second Vice-President*, Ray Grant, Brigham; *Secretary*, George F. Flashman, Salt Lake City; *Treasurer*, Walter H. Dayton, Salt Lake City. *Place of 1938 Meeting*, Ogden.

NEW OFFICERS FOR DISTRICT OF COLUMBIA PHARMACEUTICAL ASSOCIATION.

The following are the new officers of the District of Columbia Pharmaceutical Association for the year 1937: *President*, A. L. Suter; *Vice-Presidents*, J. G. Biggs, F. B. Campbell, M. Goldstein, Ralph Judd, T. A. Moskey, H. J. Werner; *Secretary-Treasurer*, W. Paul Briggs. The association meets regularly on the second Tuesday of every month.

(Reports of other associations will be published in succeeding issues of the JOURNAL.)

THE INTERNATIONAL HOSPITAL CONGRESS.

The International Hospital Congress met this year in Paris, July 5th to 11th. An interesting pre-convention program was issued, which also contains illustrations of historical and other views for the visitors. The program was well arranged and outlined the convention.

RHO PI PHI FRATERNITY.

Maurice Goldsmith, director, Public Relations and Chairman of 1937 Award Committee, advises that on July 28th, 29th and 30th, the Rho Pi Phi Fraternity, consisting of all the graduate members of the 14 leading Colleges of Pharmacy in the United States will hold its annual convention at the Hotel Statler, Boston, Massachusetts.

Members of the organization consist of doctors, surgeons, pharmacists and medical authorities who have devoted their lives to work in some division of the medical world—lawyers, congressmen, governors and writers who have taken to some other field of endeavor. The annual convention provides an excellent opportunity for old schoolmates to meet.

The highlights of the Rho Pi Phi Convention are the annual awards made "to individuals and organizations who have given the most service to humanity during the elapsed time between conventions."

Heretofore the recipients of the three awards have been chosen from the many suggestions sent to the Awards Committee by the graduate body of the fraternity. For the 1937 convention, however, it was agreed that the award recipients will be chosen from those suggestions "sent by the graduate members of the fraternity and the members of the press of the country."

William Randolph Hearst will be honored at the convention for "distinguished service." The fraternity will especially commend Mr. Hearst "for instituting 'Your Good Health' radio programs, sponsored by the *American Druggist*."

A number of awards, other than heretofore mentioned, will be formally awarded by Rho Pi Phi to those who have rendered outstanding services in various walks of life. Interesting programs have been prepared for the sessions and a memorial service will be held in memory of the late Theodore J. Bradley, former dean of Massachusetts College of Pharmacy.

MASSACHUSETTS COLLEGE OF PHARMACY.

Leon Clifton Ellis has been elected president of Massachusetts College of Pharmacy succeeding William H. Glover, who resigned after 15 years of service. President Ellis maintains a professional pharmacy in Lynn, Mass.

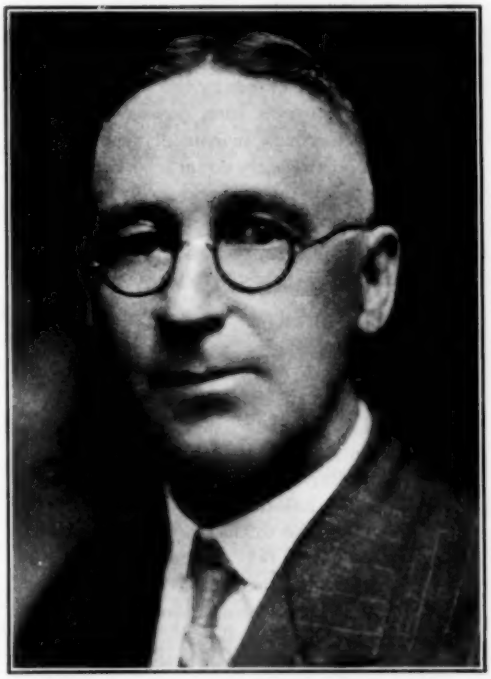
By vote of the Board of Trustees the following promotions of members of the Faculty become effective.

Eldin V. Lynn, from Associate Professor of Chemistry to Professor of Chemistry and Chairman of the Department of Chemistry.

Howard L. Reed, Ph.C., from Lecturer on Materia Medica to Assistant Professor of Pharmacology.

Leslie M. Ohmart, from Instructor in Pharmacy to Assistant Professor of Pharmacy and Special Assistant to the Dean.

Carroll B. Gustafson, from Instructor in Chemistry to Lecturer on Pharmaceutical Arithmetic and Chemistry.



Leon Clifton Ellis, President, Mass. College of Pharmacy.

William H. Glover continues as member of the Board of Trustees; William R. Acheson is *Vice-President* and Ralph R. Patch is *Auditor*.

NEW JERSEY BOARD OF PHARMACY.

The New Jersey Board of Pharmacy has issued notices to merchants relative to the sale of drugs, medicines and poisons. The information given, if observed, will prevent trouble and dealers are advised that the Board is ready to give further information if necessary.

CALIFORNIA PRICE MEASURE.

California House Bill 409, prohibiting price discrimination to certain dealers—modeled after the Federal Robinson-Patman Act.

A new section is added to the bill which provides—"Sec. 16. No manufacturer or wholesaler shall grant any advertising allowance to any retailer or other wholesaler unless: (*a*) Such retailer or other wholesaler has actually expended an amount equal to such allowance, and (*b*) Such advertising allowances are available on proportionately equal terms to all other customers competing in the distribution of such products or commodities. No manufacturer or wholesaler shall pay any retailer or other wholesaler for the use of space on the premises for the advertising or display of commodities which are offered for sale by the retailer or other wholesaler to whom such payment is made, unless such payment or consideration is available on proportionately equal terms to all other customers competing in the distribution of such products or commodities."

NEW MISSOURI LAW.

Governor Lloyd C. Stark has signed the Missouri Pharmacy prerequiste measure, House Bill 265, which was passed by the Missouri Legislature. The law will become effective on September 6th. It provides that all applicants for registration must be graduates from accredited colleges of pharmacy. The Governor has taken no action in naming four new members to the state board of pharmacy. However, before leaving on a two-week vacation in Alaska, he left instructions that no pharmacy examinations are to be held during his absence.

The St. Louis College of Pharmacy Alumni are planning a victory celebration, to be held in the auditorium of the college, to which will be invited all local drug associations and others interested in the passage of this law, the date to be announced later.

At this time a plaque will be presented to the College memorializing the student body for the part they played in calling to the Governor's attention conditions surrounding the holding of examinations to qualify persons as registered pharmacists. It is felt that the wide publicity given the conduct of the pharmacy examination had an important effect in securing the elimination of the objectionable ten-year clause, and in securing the final passage of the measure at this session.

THE WISCONSIN FAIR TRADE CASE.

C. R. D. A. News states that keeping up with the decisions of State courts on fair trade cases is becoming slightly bewildering. Just as one adopts a certain concept of the privileges and entanglements associated with a fair trade law, he finds his views disturbed by a new court decision.

Such is the case with the new declaration of the Wisconsin Supreme Court that fair trade contracts are not closely connected with the sale of goods across state lines, but merely cover resale of the merchandise by dealers within a state, and therefore fair trade contracts made between a producer in one state and retailers in a different state do not constitute transactions in interstate commerce and do not violate federal antitrust laws.

OREGON STATE PHARMACY DIRECTORY.

The *Oregon State* for June publishes a directory of the Oregon State School of Pharmacy. In the list are the activities of the alumni: it shows that more than 75 per cent of the graduates are doing work closely associated with their training.

CONNECTICUT COLLEGE OF PHARMACY.

The Connecticut College of Pharmacy has recently purchased a piece of property centrally located on York Street in New Haven. The land has a frontage of about seventy-five feet, and on it are two three-story buildings which formerly housed the Medical School of Yale University. One of these buildings has been occupied by the College of Pharmacy during the past twelve years, while the other, equal in size to the one now in use, will be used for additional class rooms and laboratories.

CALIFORNIA'S DRUG ACT.

Governor Merriam vetoed the dangerous drug bill A. B. 1253 which would have required manufacturers to mark products "substandard" if they differed from U. S. P. or N. F. or California State Board of Public Health standards. It was pointed out that if a drug item was greatly improved over the U. S. P. or N. F., it would still have to be marked "substandard" had the proposed bill received the gubernatorial signature.

OFFICERS OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 1855.

The 1855 meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION was held in New York City, September 11th–13th. President William B. Chapman was unable to attend and Henry T. Cummings, the First Vice-President, opened the sessions. Later, during the meeting, John Meakim was elected *President;* W. J. M. Gordon was elected *Recording Secretary* and William Procter, Jr., *Corresponding Secretary.*

William B. Chapman was born at Pennyback Hall, near Philadelphia, June 5, 1818. He graduated from Philadelphia College of Pharmacy in 1834 and moved to Cincinnati in 1835. Here he was a member of the firm of Eberly & Chapman until 1839, when he started business on his own account at Sixth and Walnut Streets, and subsequently at the corner of Court and Vine Streets. When the Mechanics' Institute was completed, he opened a store in that building, which was long identified with his name. In 1839 he received the degree of M.D. from the Ohio Medical College.

Dr. Chapman became a member of the AMERICAN PHARMACEUTICAL ASSOCIATION in 1852, and was elected its president at the meeting in Cincinnati, in 1854.

During the war between the States, he was appointed Surgeon of the United States Army, being stationed at Camp Dennison.

In 1872 he was elected Professor of Pharmacy in the Cincinnati College of Pharmacy and, later, was appointed by the Court of Common Pleas, a member of the Pharmaceutical Board of Examiners. He died in Cincinnati, October 10, 1874. At the time of his death, he was the oldest pharmacist in Cincinnati and was highly regarded by the profession.

This page was prepared for the President of the New York Meeting and the references to the other officers are brief.

Henry T. Cummings, of Tacoma, Washington, joined the AMERICAN PHARMACEUTICAL ASSOCIATION in 1853.

He was born at Yarmouth, Me., November 12, 1822. After studies at Bowdoin College, he entered Harvard Medical School, from which institution he was graduated with honors. His deafness persuaded him to discontinue the practice of medicine and he then entered the drug business. He was deeply interested in pharmacy—one of the organizers of Maine Pharmaceutical Association, and took an active part in the advancement of the profession. He was one of the first Commissioners of Pharmacy in Maine.

A severe illness, in 1891, left him practically an invalid, but a change of climate benefited him very much. He died in Tacoma, December 15, 1901.

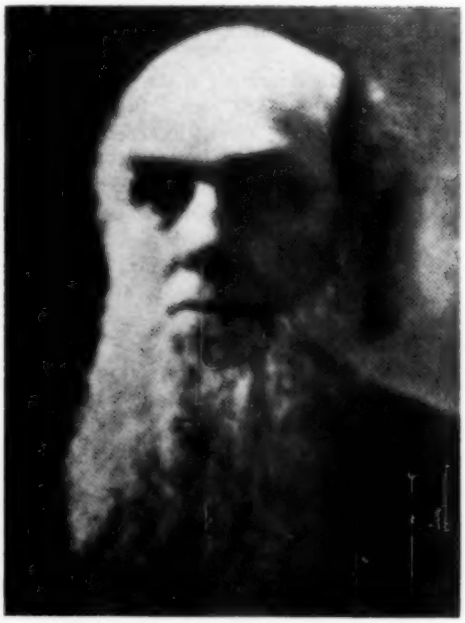
John Meakim was born in New York City in 1812 and as a young man obtained a position in the apothecaries' department of New York City Dispensary and, in 1836, graduated from New York College of Pharmacy. Until 1840, he was employed with Rushton & Aspinwall, when he engaged in business on his own account, continuing until the day of his death. He was one of the original members of the AMERICAN PHARMACEUTICAL ASSOCIATION, and was elected its president at the New York Meeting in 1855. He died October 17, 1863.

William John Maclester Gordon was born in Somerset County, Maryland, December 25, 1825; he died at Mount Airy, Cincinnati, Ohio, July 7, 1909. He joined the AMERICAN PHARMACEUTICAL ASSOCIATION in 1854 and continued as member for 55 years. He served as *Recording Secretary* from 1855–1859; as *Vice-President,* 1860–1862, and as *President,* 1864–1865. He was vice-chairman of the Council in 1881–1883.

For many years he was engaged in the manufacture of glycerin—see page 1119, December JOURNAL, 1925.

William Procter, Jr., "Father of American Pharmacy," was born in the City of Baltimore, May 3, 1817. He died on the morning of February 10, 1874. At the Richmond meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION, in 1900, a Memorial Address was delivered by the late Joseph P. Remington and remarks were made in memory of William Procter, Jr., by others—see PROCEEDINGS of 1900, pages 12–32. The Address was reprinted and will serve the purpose far better than brief remarks by this writer. A memorial will be placed in the AMERICAN INSTITUTE OF PHARMACY.

Henry T. Cummings, Portland, Maine, *Vice-President*, A. PH. A., 1854–1855, presided at New York meeting, owing to absence of President Chapman.



William B. Chapman, Cincinnati, Ohio, *Corresponding Secretary*, 1853–1854. *President*, A. PH. A., 1854–1855.

W. J. M. Gordon, Cincinnati, Ohio, *Recording Secretary*, 1855–1859. *President*, A. PH. A., 1864–1865.

William Procter, Jr., Philadelphia. "Father of American Pharmacy."

Elected *Corresponding Secretary* at New York meeting. *President*, A. PH. A., 1862–1863.

John Meakim, New York, N. Y. Elected *President*, A. PH. A., 1855, at New York City meeting, September 11th.